THE AMERICAN SURGEON

Presidential Address
THE IMPACT OF SURGERY ON THE SURGICAL MAN

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As a prudent preliminary step, I have reviewed the presidential addresses of many distinguished surgeons. Most of them have discussed parasurgical topics or subjects of nonsurgical personal interest. Such essays have included the effects of surgery upon society, the many historical facets of surgery, surgical education, surgical scientific advances and even some of the tall tales of surgery. There is a great temptation on an occasion like this to indulge in reminiscence; to review the accomplishments of the past and other external signs of progress and advancement. Certainly, these things are valid grounds for some sense of satisfaction but, reviewed in their perspective, they are secondary to the impact of surgery on you, as surgical men. This is less well explored and assessed. It is this subject that I have selected, for there are few better podiums from which this sort of essay may be presented.

It seems to me the business of being a surgeon is a process which has evolved out of aspiration, extensive undergraduate studies, long graduate training influenced by men of stature and, most of all, by the experiences obtained at the patient's bedside and in the operating room.

In making the choice of a surgeon's career, one has passed through a complex pattern of intellectual, emotional and practical considerations, and has gained a substantial foothold on the lower rungs of becoming a surgical man.

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Delivered before the 27th Annual Assembly of the Southeastern Surgical Congress, March 9, 1959.

What are some of the considerations of a man who elects the surgical path? A basic requirement must be the possession of physical dexterity, coupled with an innate fascination for artisanship: deriving recurring pleasure from an accurate repair of torn tissue or fractured bones, in the deft anatomical dissection of diseased areas and the skilful reapproximation of functional parts.

A second consideration is having, as a driving force, an investigative bent for resolving obscure pictures and syndromes in a clear-cut fashion without delay.

Third, is a willingness to assume responsibility. This is necessary for positive action in recommending and implementing a surgical attack on diseased processes.

A fourth attraction, in common with all physicians worthy of their profession, is the appeal to the compassion in a man. It is the desire to succor humanity when in physical and mental distress, with resultant dedication of the physician's heart, mind and hand through the surgical approach, for relief or cure, by knowledge, observation and investigation.

A fifth consideration that, I hope, is of minimal significance but which, at times, may be a compelling influence in seeking to be a surgeon, is its reputed glamor. There is no doubt that, sometime in most young medical students' lives, the surgeon has had a romantic appeal. Motion pictures, television and printed stories have done little to discourage such an effect, with their views or descriptions of the quiet operating room, gleaming instruments, silent masked figures efficiently carrying out the orders of what appears to be a Supreme Commander with scalpel in hand. Lost

to the neophyte is the weight of responsibility, the occasional errors in judgment or the painful lack of current knowledge to control the disease process. While so-called glamor has remained a facet in the routine of doing surgery, those of us now tried by the fire of practice no longer have such an illusory compensation for the poignant moments of remorse, self-condemnation and soul-searching. We, rather, seek the peace of understanding which comes from other qualities yet to be mentioned. Tried and true surgical physicians enjoy a different kind of daily drama, unknown to scenario writers and authors. This is a mental excitation in the prospect of the action which lies immediately ahead: the opposing of the unknown with knowledge, judgment and skilful dexterity. The storytellers are not aware of the drama in the lull before the operation, when preparation of the patient and surgeon causes a necessary pause: a quiet drama of the mind, when composure is apparent but tensions exist; when compassion for the patient and the necessity of procedure are in conflict, and must be resolved promptly.

To have been swayed by most of these considerations in selecting a surgical career has proved essential. But to have been triumphant in implementing the practice of surgery, one must have striven for excellence. As Jacques Barzun, Dean of Faculties at Columbia University, has said, "Excellence means excelling, which means exerting the will to improve on nature according to rule. To squeeze high performance out of native ability, stern demands must be made by the talented on themselves, but these demands must come, ultimately, from the world that desires and rewards the performance." Excellence in education implies intellectual attainment. Intellect is a possession which, when disciplined by favorable scholastic environment and teachers of scholarly stature, brings to the budding surgeon growing mental powers which begin to play outward, until, at length, he loves the task at hand, not because it gains him a livelihood, but because it makes him a life.

Intellectual pursuits add immense interest for the surgical man while he lives in the midst of practical problems which confront him. The disciplines involved in intellectual excellence in surgical practice demand a price of sacrifice, pain and acceptance of failure and humiliation, at times. But, from such a crucible, certain rare and precious qualities are distilled which grow within him. Not all of us may be fully dominated by

such qualities, for we are human. But let us be thankful that the life we lead tends to cultivate our nobler characteristics, rather than the littleness that shadows our very being.

The first quality which the surgical man possesses, distilled from training and experience, is *intellectual curiosity*. He has made outstanding contributions in unraveling the secrets of the human body. Intellectual curiosity has been a stimulus to broaden man's knowledge of human disorders and to discover clues for correcting them. "In the progress of knowledge," said Sir William Osler, "each generation has a double labour, to escape from the intellectual thralls of the one from which it has emerged, and to forge anew its own fetters." Who could be more deeply concerned about the progress of knowledge than the surgeon who realizes imperfections of treatment, despite his information about disease processes and his technical skills? And who can deny the contributions of such men as Paré, Kocher, Lister, Halsted and a host of others? Such men have contributed to the knowledge of antisepsis and asepsis, to the progress of surgical techniques, organ physiology, fluid replacement, the use of chemotherapeutic agents, the control of neoplastic diseases, employment of tissue replacement and many other advances. The membership of our own Congress contains those whose study of physiology, both normal and abnormal, has been illuminating to the whole field of medicine. I hope the day will soon come when we of the South can look to this organization as a beacon of intellect, second to none, taking its place with the distinguished surgical societies of this country and with membership even more desirable to attain, but difficult of attainment.

A second quality found in the distillate from the crucible of training and practice is *intellectual honesty*. A surgeon or physician does not deserve to bear the name if this quality is lacking. Nothing shrivels the soul and mind more quickly than creating about one a chilly fog of dishonest representations. Confession of error and ignorance has proved good for the soul, and an honest appraisal of mistakes, with acknowledgment of them, represents a pattern of commendable behavior. Surgical men have come to themselves by discovering their limitations, no less than by discovering their deeper endowments.

The third quality emanating from the crucible of surgical experience is *equanimity*. The word means coolness and presence of mind, imper-

turbability and, withal, serenity of demeanor. It is a priceless possession to be enshrined in the makeup of any individual, and brings comfort to all who have come in contact with the man or woman endowed with it. To quote from Osler's essay, "Aequanimitas," "It is the quality which is most appreciated by the laity, though often misunderstood by them; and the physician who has the misfortune to be without it, who betrays indecision and worry, and who shows that he is flustered and flurried in ordinary emergencies, loses rapidly the confidence of his patients. . . . In a true and perfect form, this imperturbability is indissolubly associated with wide experience and an intimate knowledge of the varied aspects of the disease. . . . Keen sensibility is doubtless a virtue of high order, when it does not interfere with steadiness of hand and coolness of nerve."

The fourth quality in the distillate I wish to discuss is *faith*. It has been born of confidence and trust; it walks hand-in-hand with belief in the reality of God as the creator of the universe and of all humanity. It follows, inherently, that we have faith in ourselves, in the best of the past and in hope for the future. It has been said that mankind is always advancing; man is always the same. "The love, hope, fear and faith that make humanity, and the elemental passions of the heart, remain unchanged" (Osler). Faith in the future acts as a beacon by which we perceive the broader meaning of life. It casts a beckoning glow, encouraging us to advance and participate in unraveling the processes of mental and physical distress. It creates in us a dedication to pay our debts to the past by putting the future in debt to us. Faith is reciprocal in those whom, ultimately, we are privileged to serve.

Courage is the final quality from the distillate of experience which goes hand-in-hand with faith and equanimity, and shores up complete intellectual curiosity and honesty. Courage is a quality of mind which enables the individual to face difficulties with fearlessness, daring, fortitude and intrepidity. It is unadorned decision, born of limited time to think, or decision made in the lonely quietness of one's consciousness. It is the quality which inspires responsibility for action. Surely there is no profession which so often requires calm, reasoned courage wrung from the depths of the best that is in a man.

Although the impact of a medical education, postgraduate surgical training and the ultimate practice of surgery fosters these fine traits of character in a surgeon, it does not inevitably develop the qualities to which he may aspire. Let me point out, however, with Isaiah Bowman, the late illustrious president of Johns Hopkins University, that "some of your less desirable qualities go back at least to the Ice Age and may seem to you discouragingly stable. Some, happily, are subject to your own control. Great ideals require nourishment or they die within you. They grow and flourish according to your reading, your company, your belief in the power of the individual to deflect, if only by a little, the forces of life, to make a work towards a design for living. That design is subject to endless revision."

Work of *quality* determines the surgical man's rank among his colleagues and the world at large. Quality may be defined as a striving for not merely skill, but mastery. In effect, it is another form of striving for excellence. "It is emulation of great work, that the magic of it may, perchance, be wrought in some measure through you, again. It is not acquired by tricks or formulae. It grows out of a profound conviction about the worth of your life and what you can make of it . . ." (Bowman).

Through the years of my recollection, the surgical man has been subjected to changing concepts of medical education, training and practice. He has seen the stresses and strains of world wars and cold war. He has seen inflation. He has seen the specter of socialization of our profession come to fruition in other countries. He hears the ominous moaning of this apparition in the reaches approaching the citadel of American medicine. What have these impacts done to the surgical man, and what of tomorrow?

I am sure that another quality from the crucible of experience will be this, namely, *adjustment*. The surgical man is made of stuff that will shake into shape and fitness and reveal a durable warp and weft. These new problems are certainly tasks to be solved. Some are left to statesmen. Some are within the surgical man's reach for direct action. His aggressive character will not be found wanting in such circumstances. He must look with zest towards the future, maintaining his basic qualities and good traits, but adjusting to the ever changing new adventure; seeking compromise where he can; directing thoughts of statesmen where he may, in bettering the health of all men but, at the same time, seeking to preserve an equitable way of life for those who serve in the professional care of the sick.

The late Charles F. Kettering had a characteristic saying, "We are not at the end of our progress, but at the beginning. We have but reached the shores of a great unexplored continent. We cannot turn back. . . . It is man's destiny to ponder on the riddle of existence and, as a byproduct of his wonderment, to create a new life on this earth. . . . I think it is all right," he said, "to have courses in history. But history is the 'gonest' thing in the world . . . . Let's keep history, but let's take a small part of the time and study where we are going . . . . We can do something about the unmade history."

Differing points of view and conviction regarding quality of achievement and how accomplished "helps create in each educated man of us the something distinctive and personal that compels him to chase those rainbows which he calls ideals, knowing in advance that he will never come to the end of the chase, but believing that he will find something precious on the way. . . . No one can close his mind to the value of rival points of view, however they may clash with his prejudices and dare to say, thereafter, that he is an educated man" (Bowman).

Having established what qualities and stability the surgical man has achieved through the impact of surgery on his life, let us remember that surgical men know each other's trials and know that each has cultivated a modicum of nobility inherent in the surgical art. We are drawn together in a bond of professional association by common problems and methods of solution. The "ethos" of a surgical career should encompass the philosophy of our total education and of our way of life, which embraces the whole man, body and spirit, that looks to the total purpose of man's life here on earth and hereafter. *Advance* should be our final watchword. The method of advance

to which I subscribe is beautifully expressed in the words of my late colleague and classmate, Royall Frazier:

That priceless dream or vision
Or awakening something
Which stirs the heart to restless yearnings
For heights and steps untrod,
And wakes the slumbering
Force that holds the destiny
Of one's whole life
And reveals to him the hidden
Purposeful ideals towards
Which he struggles in the face
Of defeat and failure—
Harboring faith and hope,
Pushing through peril,
Suffering stings and sacrificing
Self to attain the goal—
Is the thing in which is locked
The force that advances humanity
Toward the higher purposed end.

But these yearnings in most men
Are no more than rippling waters
That follow the course of the stream,
In the midnight silence
Of the moonlit night,
Over the impelling precipice
And fall to the pool below,
Making for a moment
The unseen silvery foam
Which soon disappears forever
As a dream that is only dreamed.
But in those few whose hearts hold
Dreams full of purpose and beauty—
Who live by the light therein
While fearlessly fighting on
Into the vision beyond
Where lies the ideal—
There is the power of Advance.

—Royall Frazier

CARCINOMA OF THE COLON IN YOUNG PEOPLE*

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Carcinoma of the colon in young people is an unusual condition, and a review of the reported cases seems to indicate an almost hopeless prognosis. The purpose of this presentation is to bring up to date a statistic appraisal of this entity and to present two new cases. It would appear that this is not as rare as has been supposed and that the prognosis, although poor, is not necessarily hopeless.

The standard pediatric textbooks and some recent symposia on malignancies in children make little or no reference to gastrointestinal tract carcinomas, but in recent years a number of these cases has been reported in the literature. For the purpose of this review, our attention will be focused only upon those carcinomas occurring in the first two decades of life in the portion of the colon above the rectosigmoid level.

An article on carcinoma of the colon in childhood was published by Johnston[13] in 1947, including a detailed list of 48 reported cases in subjects less than 17 years old. With slight modification, this list has been expanded in the present study to include a total of 88 cases of carcinoma of the colon occurring before the age of 20 (see table 1). Statistic reports of colon lesions from several medical centers include other cases that would fall into this age group, but do not give enough information on the individual cases to include them in this table.

A review of the records at John Gaston Hospital (the teaching hospital for the University of Tennessee) from 1940 to the present failed to produce any cases which could be added to this group, but 2 such cases have been treated at the Baptist Memorial Hospital in Memphis within the past few years.

CASE REPORTS

Case 1. R. T., a 16-year-old white girl, was admitted to Baptist Memorial Hospital on February 26, 1948, with a history of recurrent attacks of cramping abdominal pain of about 2½ months' duration. Approximately 2 weeks before admis-

sion an appendectomy had been performed in another hospital, without any improvement in symptoms. At the time of admission to this hospital she presented the clinical manifestations of acute intestinal obstruction, and exploratory laparotomy on the day of admission revealed a firm, annular constricting lesion in the hepatic flexure of the colon. The lesion was thought to be resectable, but the surgeon did not consider the patient to be in good enough condition to tolerate resection at this time. Consequently, a cecostomy was done to decompress the bowel for definitive resection at a later date. The patient had a prolonged and stormy convalescence and not until May 15, 11 weeks after admission, was it considered advisable to attempt a definitive operation. At that time the bowel was still partially obstructed and a hard, fixed, irregular lesion was found to extend from the hepatic flexure to the cecum. Numerous small, slightly elevated, firm lesions were found on both parietal and visceral peritoneal surfaces. Several large, firm nodules were found in the mesentery of the bowel and one of these was excised for microscopic examination. Since the patient was not completely obstructed at this time it was not felt that any further surgery was advisable.

Microscopically, the lesion was characterized by large clear spaces with small hyperchromatic cells occurring singly and in chains (fig. 1). Most of the cells had a centrally placed nucleus, but a few had a "signet-ring" appearance. Mitoses were rare and there was rare abortive gland formation. The microscopic diagnosis was mucinous adenocarcinoma, grade III.

Following an essentially uneventful postoperative recovery, the patient was discharged on the 8th day. She was given a supply of narcotics for use at home and died soon after discharge, approximately 6 months after the initial onset of symptoms.

Case 2. J. H. W., a 14-year-old white boy, was admitted to the surgery service of Baptist Memorial Hospital on July 2, 1954, with a history of intermittent pain and fulness of the abdomen with occasional nausea and vomiting and increasing constipation for 2 months. During this time he received treatment, without relief of symptoms for "worms" and a "virus." At another hospital he had an abdominal operation at which time an

TABLE 1

Reported cases of carcinoma of colon in persons less than 20 years of age

No.	Year	Authority	Age	Sex	Location	Microscopic Diagnosis
1*	1865	Steiner	9	M	Sigmoid	Alveolar epithelial carcinoma
2	1872	Leijer	9	M	Sigmoid	Alveolar epithelial carcinoma
3	1878	Spanton and Frost	12	F	Cecum	Encephaloid carcinoma
4	1883	Maydl	12	F	Cecum	?
5	1883	Maydl	13	M	Cecum	?
6	1885	Clar	3¼	M	Sigmoid	Carcinoma
7	1893	Burger	15	M	Ascending colon	?
8	1895	Mayo-Robson	14	F	Ascending colon	Columnar epithelioma
9	1897	Garrard	12	M	Sigmoid	Colloid carcinoma
10	1897	Petroff	16	M	Hepatic flexure	Carcinoma
11	1898	Nothnagel	12	M	Cecum	?
12	1898	Israel	13	M	Splenic flexure	Colloid carcinoma
13†	1900	Paultauf	12	F	Sigmoid	Cylindric cell epithelioma
		Zuppinger	12	F	Sigmoid	Cylindric cell epithelioma
14	1902	Marsh	15	M	Sigmoid	Columnar cell carcinoma
15	1904	Ruczynski	13	M	Splenic flexure	Cylindric epithelioma
16	1906	Madelung	13	M	?	?
17	1907	Allbutt and Rolleston	10	M	Sigmoid (?)	Colloid carcinoma
18	1907	Bernouilles	15	M	Sigmoid	Alveolar carcinoma
19	1908	Clogg	15	?	?	?
20	1913	Muralt	13	M	Ascending colon	Colloid cylindric epithelioma
21	1913	Parkinson	9	M	Sigmoid	Colloid carcinoma (?)
22	1921	Olmsted	14	M	Sigmoid	Adenocarcinoma
23	1923	Mouchet and Baranger	10	F	Splenic flexure	Adenoepithelioma
24	1925	Wainwright	11	F	Splenic flexure	Gelatinous carcinoma
25	1925	Ulhorn	3½	M	Sigmoid	?
26	1926	Clark	16	M	Sigmoid	Carcinoma
27	1929	Chajutin	14	F	Cecum	Adenocarcinoma
28	1930	Drinkwater	15	F	Descending colon	Colloid carcinoma
29	1931	Rocher and Guerin	11	M	Splenic flexure	Adenocarcinoma
30	1933	Walker and Daly	5	M	Cecum	Adenocarcinoma
31	1933	Pouzet	14	M	Ascending colon	Adenocarcinoma
32	1933	Wakeley	16	M	Ascending colon	Colloid carcinoma
33	1935	Pfeiffer and Wood	7	M	Transverse colon	Fibroma with adenocarcinoma
34	1935	Stuart	15	M	Transverse colon	Carcinoma
35	1935	Ball	15	F	Sigmoid	Mucoid carcinoma
36	1935	Ogilvie	13	M	Cecum	Mucoid carcinoma
37	1937	Warthen	14	F	Transverse colon	Signet ring adenocarcinoma
38	1938	Webster	9	F	Sigmoid	Adenocarcinoma
39	1938	MacQuire	15	M	Transverse colon	Adenocarcinoma
40	1940	Rawls	12	F	Splenic flexure	Colloid carcinoma
41	1940	Plehn	9	F	Cecum	?
42	1941	Pennell and Martin	13	M	Ascending colon	Colloid carcinoma
43	1941	Laird	14	M	Splenic flexure	Colloid carcinoma
44	1943	Moes and Dittmer	16	M	Transverse colon	Adenocarcinoma
45	1943	King	12	M	Sigmoid	Colloid carcinoma
46	1944	Sandes	12	M	Ascending colon	Colloid carcinoma
47	1946	Johnston	13	M	Transverse colon	Adenocarcinoma
48‡	1879	Dubar[21]	19	M	Sigmoid	Colloid
49	1919	Barber[2]	19	M	Sigmoid	"Typical carcinoma"
50	1934	Rosenberg[14]	16–20	M	(Colon)	?
51	1934	Rosenberg[14]	16–20	F	(Colon)	?

TABLE 1—*Concluded*

No.	Year	Authority	Age	Sex	Location	Microscopic Diagnosis
52	1934	Rosenberg[14]	16–20	M	Sigmoid	?
53	1935	Netto[14]	10	F	? (Colon)	Adenocarcinoma
54	1946	Scholefield[25]	17	M	Splenic flexure	"Ring carcinoma"
55	1946	Saner[24]	11	F	Transverse	Mucoid
56	1947	Fishback[8]	15	M	Transverse	Colloid
57	1947	Bellone[4]	19	M	Sigmoid	?
58	1948	Kerr[17]	12	M	Sigmoid	(Possible pre-existing polyp)
59	1949	Nelson and associates[19]	14	M	Right colon	Adenocarcinoma with mucoid degeneration
60	1950	Read[22]	17	M	Splenic flexure	Papillary
61	1952	Newns and Donald[20]	10	M	Descending colon	Adenocarcinoma
62	1954	Williams[31]	12	M	Hepatic flexure	Colloid
63	1954	Williams[31]	15	M	Splenic flexure	Colloid
64	1954	Williams[31]	12	F	Hepatic flexure	Colloid
65	1958	Hoerner[12]	18	M	Sigmoid	Adenocarcinoma
66	1897	Kanthack and Furnivall[15]	17	M	Ascending colon	Colloid
67	1923	Phifer[21]	19	M	Sigmoid	Columnar carcinoma
68	1932	Karsner and Clark[16]	19	M	(Colon)	?
69	1933	Abell[1]	19	F	Cecum	Colloid
70	1933	Abell[1]	17	M	Transverse colon	Colloid
71	1937	Stebbins and Burke[28]	18	M	Sigmoid	Adenocarcinoma
72	1937	Ritvo and associates[23]	15	F	Descending colon	?
73	1939	Klemt[18]	10	F	Descending colon	Colloid
74	1939	Klemt[18]	13	M	Ascending colon	Colloid
75	1949	Lagercrantz[30]	15	M	? (Colon with liver metastasis)	(Ulc. colitis)
76	1950	Mallory[30]	12	F	Transverse colon	(Ulc. colitis)
77	1953	Gross[10]	13	M	(Colon)	(Ulc. colitis)
78	1955	Bargen and Kennedy[3]	17	?	Right colon	(Ulc. colitis; grade IV multicentric) (carcinoma)
79	1955	Wheeling and Warren[30]	14	?	(Colon)	(Ulc. colitis)
80	1956	Bargen[30]	15	?	(Colon)	(Ulc. colitis)
81	1956	Wilcox and Beattie[30]	11	F	Cecum	(Ulc. colitis)
82	1956	Heller and associates[11]	9	F	Hepatic flexure	Mucus-secreting
83	1958	Fitch and Denman[9]	17	M	Descending colon	Adenocarcinoma
84	1958	Buchman and Calhoun[6]	15	M	Sigmoid	Mucoid
85	1958	Buchman and Calhoun[6]	13	F	Splenic flexure	Mucoid
86	1958	White and associates[29]	9 mo.	F	Hepatic flexure	Mucus-secreting
87	1959	Chappell	16	F	Hepatic flexure	Mucinous
88	1959	Chappell	14	M	Descending colon	Adenocarcinoma

* Data on cases 1 though 47 are taken from Johnston's article.[13]

† According to Shedden,[27] Zuppinger's case is the same one reported by Paultauf.

‡ Cases 48 through 65 are mentioned in Hoerner's article,[12] but details were taken from other sources as indicated. Hoerner also mentioned a case reported by Chauvenet,[7] which, on reference to the original article, was found to be a carcinoma of the small bowel.

obstructing lesion of the colon was found, and a tube cecostomy performed. Postoperatively he remained partially obstructed and became progressively weaker until transfer to this hospital 4 weeks after surgery. Except for a functioning tube cecostomy and general evidence of chronic disease the physical examination on admission was not remarkable. Laboratory studies were within normal limits. A barium enema x-ray revealed a complete obstruction about 10 cm. below the splenic flexure, with gaseous distention of the bowel proximal to this point (fig. 2). After prepa-
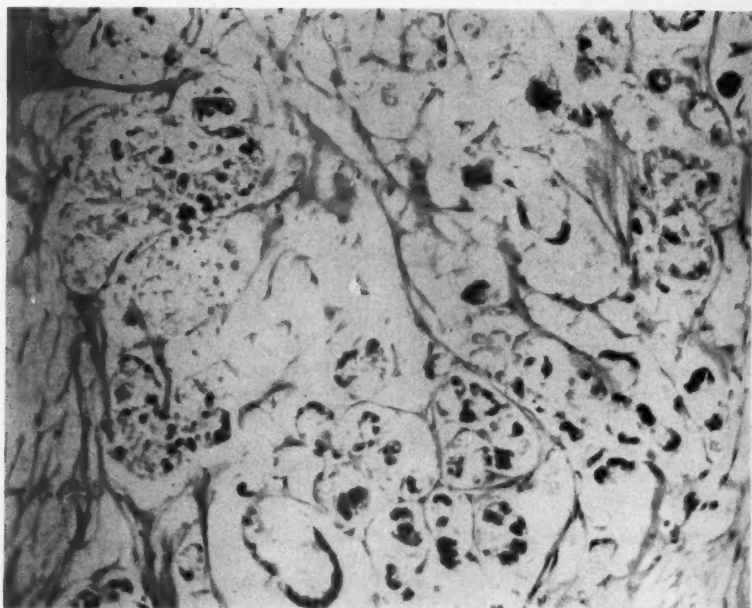
Fig. 1. Photomicrograph of specimen from case 1

Fig. 2. Preoperative barium enema x-ray from case 2.

ration with Sulfathalidine and neomycin, a laparotomy was performed, on July 10, approximately 6 weeks after the initial surgery. Extensive adhesions were found throughout the peritoneal cavity, but there was no evidence of metastatic tumor in the liver or mesentery. A block resection of the primary lesion in the mid-descending colon was performed, including the segment of colon from the mid-transverse to the upper sigmoid level. Intestinal continuity was re-established with a 2-layer end-to-end anastomosis and the abdomen was closed without drainage.

The resected specimen was a segment of colon 27 cm. in length, with a circular fungating ulcerative lesion located 8 cm. from one margin of resection, involving the entire circumference of the bowel. Microscopically (fig. 3) it was a moderately well differentiated adenocarcinoma which extended through the entire thickness of the bowel wall and into the adjacent mesentery. Many of the cells were mucus-producing and there was a significant amount of mucus within the malignant glands. No blood vessel invasion was demonstrated and 33 mesenteric nodes were negative for metastatic carcinoma. The diagnosis was adenocarcinoma of the colon, grade II.

The patient made a satisfactory postoperative recovery, with the cecostomy closing spontane-
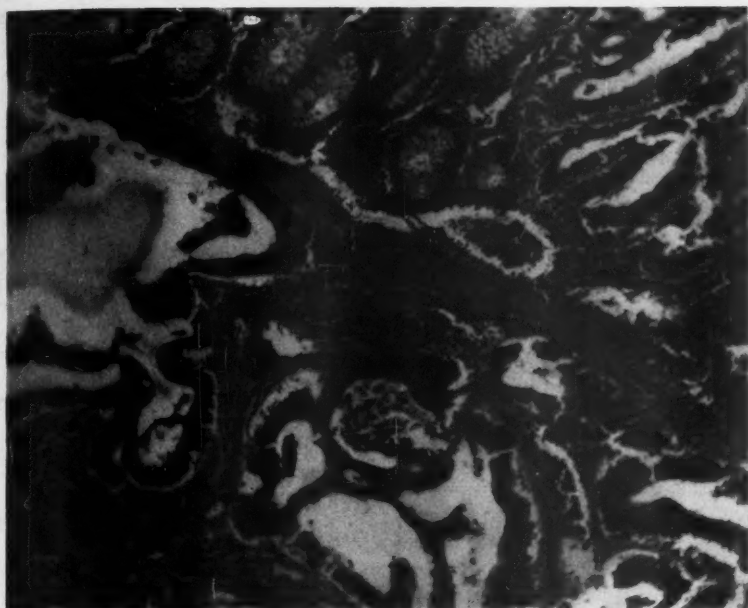
FIG. 3. Photomicrograph of specimen from case 2

FIG. 4. Barium enema x-ray from case 2 made 15 months after the primary resection.

ously on the 9th day. He was discharged from the hospital on the 15th postoperative day, at which time he weighed 89 pounds.

He was seen at regular intervals in the outpatient department, and remained asymptomatic. Two barium enema x-rays were reported as normal and within about 15 months he had gained 67 pounds. A third barium enema at this time, however, revealed about 60 per cent reduction of caliber of the bowel lumen at the anastomotic site (fig. 4). Proctoscopic examination was negative for a distance of 14 cm.

The patient was readmitted to the hospital and after preparation with Sulfasuxidine an exploratory laparotomy was performed on October 18, 1955. At the site of anastomosis there was a firm constricting mass, presumably carcinoma. No metastases were demonstrated in the liver but several nodules were found in the omentum, measuring up to 1.5 cm. in diameter. In addition, multiple small, white, firm nodules were scattered diffusely over the visceral and parietal peritoneal surfaces. One of the nodules in the omentum was excised for microscopic examination and a side-to-side anastomosis was made between the transverse colon and the sigmoid. Microscopic examination of the nodule revealed adenocarcinoma, grade II. The postoperative

course was uneventful and the patient was discharged on the 11th day.

Following discharge, the patient felt well and resumed his usual activities, without symptoms of disease, for about 6 months. He was last seen in the outpatient department on May 10, 1956. At this time he complained of severe constipation, frequent vomiting, abdominal pain, progressive weakness and weight loss. On rectal examination a firm, nontender mass was found filling the cul-de-sac. Arrangements were made for sedation and other terminal care at home, where he died approximately 2 years after the first onset of symptoms.

Fig. 7. Primary site of carcinoma of the colon (78 cases).

DISCUSSION

Although cancer of the colon is usually considered to be a disease of older people, it is evident from the cases reviewed here that it may occur even in the very young (fig. 5). For many years Clar's 3-year-old patient was regarded as the youngest recorded case.[12, 13] In 1958, however, White and associates[29] reported a case of adenocarcinoma of the descending colon in a 9-month-old girl. The greatest number of cases occurring in the first two decades of life is in the 10- to 14-year-old group. This would seem to be related to the increased growth rate and other physiologic changes normally occurring at the age of puberty.

Cancer of the colon (excluding the rectum) in adults is slightly more common in females, but it was found to occur more frequently in males in this series of patients below the age of 20. Of 84 cases in which the sex was indicated, 58 (69 per cent) were males (fig. 6).

The portion of the colon most commonly affected by carcinoma is the sigmoid, the site of 24 of the 78 lesions which were accurately localized in this series (fig. 7). It has been supposed that the character of the bowel content at this point, with stasis and chronic mechanical irritation, may account for the increased frequency of carcinoma here. This would also seem to account-

Fig. 5. Incidence of carcinoma of the colon in age groups of less than 20 years (88 cases).
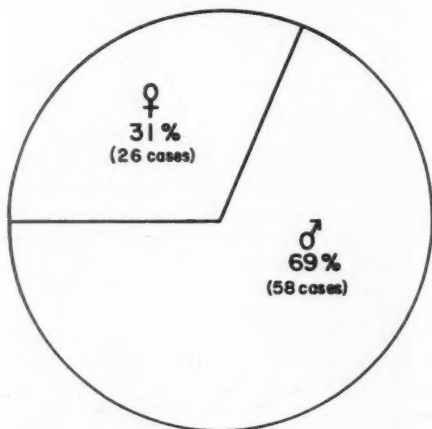
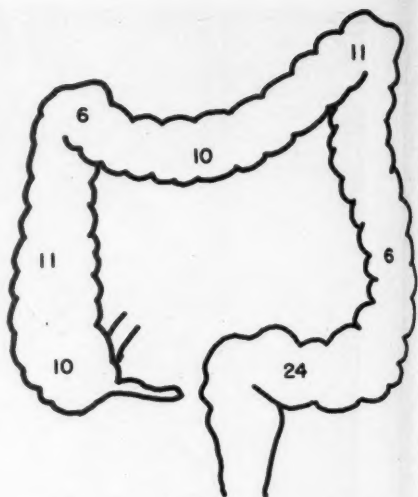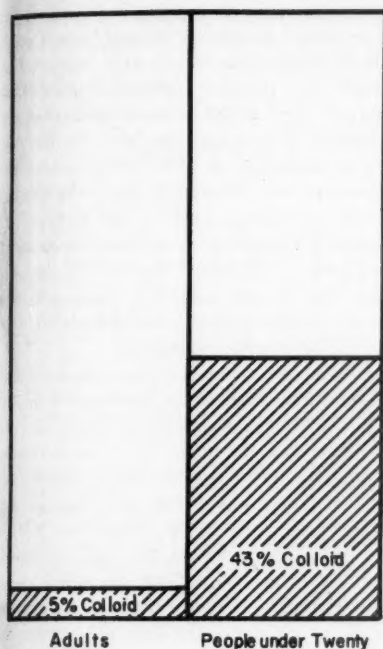Fig. 6. Sex incidence of carcinoma of the colon in young people (84 cases).

Fig. 8. Relative incidence of "colloid" lesions in adults and young people.

for the fact that carcinoma of the rectum is much more common than carcinoma of the colon, with a ratio of 3 to 1 in adults, and 2.5 to 1 in individuals before the age of 20.[12]

It has been pointed out by many authors that the carcinomas occurring in young people are more highly malignant than those found in older patients. Although pathologic details are lacking in many of the cases reviewed, there was found to be a high incidence of the tumor type referred to as "colloid," "mucinous," or "gelatinous." Of the 73 cases in which the pathologic type was indicated, 32 (43 per cent) were of this variety (fig. 8). In contrast, colloid carcinomas make up less than 5 per cent of colon carcinomas in adults.[6, 13, 31] It is true that the production of large amounts of this mucinous substance indicates a fair degree of differentiation in the tumor, thus giving it a lower degree of malignancy according to the Broders classification. Nevertheless, this colloid material seems to act as a sort of dissecting wedge facilitating the early and extensive spread of the tumor cells through adjacent tissue planes, so that the prognosis for this type of tumor appears to be worse than for some of the more undifferentiated types.

At the present time the prognosis for carcinoma of the colon in children is very poor. No cures have been confirmed in the patients treated before the age of 16 years, the longest survival in this group being a girl reported by Webster[13] who died of a cerebellar metastasis 4 years following her initial treatment. She had been treated at the age of 9 years by a Miculicz resection of an adenocarcinoma of the sigmoid colon. Apparent cures have been reported in 2 patients treated between the ages of 16 and 20 years. In 1946 Scholefield[25] reported a 7-year survival in a youth operated upon at the age of 17. His initial treatment was a cecostomy performed for relief of obstruction, followed in 3 weeks by resection of a carcinoma of the splenic flexure. This patient has since been reported to be alive and free of symptoms more than 18 years after surgery.[26] Hoerner[12] reports a case of a highly malignant adenocarcinoma of the sigmoid treated by primary resection in an 18-year-old male. Although one lymph node was almost completely replaced by metastatic tumor, this patient was alive and had a normal colon x-ray 8 years later. A number of other cases has been reported free of evidence of disease 6 months to 1 year following surgery, but no other long term survivals have been confirmed.

It has been stated that when cancer of the colon is encountered before the 4th decade of life it is usually on the basis of multiple polyposis or of ulcerative colitis. Interestingly enough, none of these 88 cases of carcinoma of the colon seemed to be associated with multiple polyposis. Although it is generally recognized that a significant proportion of patients with untreated familial polyposis will develop carcinoma before the age of 40, it is apparently unusual for the malignancy to become manifest before the age of 20. (There are reported cases of such malignancies in the rectum occurring in childhood, however.[10])

In this review, 7 cases of carcinoma developed as a complication of ulcerative colitis.[3, 10, 30] Statistics indicate a definitely higher incidence of malignancy in those individuals who develop ulcerative colitis before the age of 20 than in those who develop it later.

The possibility of carcinoma's arising in a previously benign solitary polyp has been the

subject of considerable speculation and debate. In only one of these cases was there evidence to indicate the presence of a polyp before the development of carcinoma; this was in a 12-year-old boy with carcinoma of the sigmoid who gave a history of repeated episodes of cramping lower abdominal pain associated with the passage of bloody mucus since the age of 3 years.[17] There is an interesting correlation between the occurrence of polyps in 92 children reported by Gross[10] and the incidence of carcinoma in the present series. The sex incidence is similar (58 per cent of the patients with polyps were males, 69 per cent of those with carcinoma were males), whereas the peak age incidence for polyps was 5 years, approximately 7 years younger than the peak incidence for carcinoma. Although such a correlation may be only coincidental, this age difference could well be accounted for by a "latent period" in the development of malignancy in the polyps.

Considering the known malignant potential of familial polyposis and ulcerative colitis and the suspected malignant potential of solitary polyps, it would seem wise to maintain an aggressive attitude toward the treatment of these conditions in childhood. Total colectomy should be advised for all patients with familial polyposis and for all young people with ulcerative colitis if the disease is not completely controlled by medical therapy. Simple excision appears to be adequate therapy for the solitary polyps, but this should be done in all cases as soon as the diagnosis is made.

In the absence of these "premalignant" conditions the diagnosis of carcinoma of the colon in children is usually a difficult one and for this reason it seems important to review the symptomatology of the disease. The classic presenting symptoms of colon carcinoma in adults, such as constipation and blood in the stools for left colon lesions and weight loss and anemia for those in the right side, received relatively little attention in the histories of these younger patients. By far, the most frequent presenting complaint was abdominal pain. Many of these youngsters were subjected to one or several operative procedures, often for suspected appendicitis, before the diagnosis was established or even suspected. One patient, a 17-year-old boy, was subjected to five abdominal operations before the diagnosis of carcinomatosis was established, and the primary constricting lesion in the splenic flexure was demonstrated only at autopsy.[22] Many of the cases presented themselves as problems of acute intestinal obstruction. Others were diagnosed on the basis of a palpable abdominal mass or an acute perforation of the colon. Aside from extensive surgical exploration, the x-ray is the best means of detecting a colon lesion above the rectosigmoid level. Therefore, any child who has persistent abdominal pain, rectal bleeding, or symptoms suggesting intestinal obstruction should have the benefit of barium enema x-ray studies. This is particularly true of the child who continues to have abdominal symptoms after the removal of a "negative appendix."

Treatment of carcinoma of the colon in children is essentially the same as the treatment in adults; that is, wide block resection to include the primary lesion and the adjacent lymphatic tissue. The poor results in most of the reported cases emphasize the importance of early diagnosis and early definitive treatment. Where possible, it seems advisable to avoid the use of "staged operations" which may delay the definitive resection. Fitch and Denman[9] reported the primary resection of a lesion of the descending colon in a 17-year-old boy in the presence of acute intestinal obstruction. This patient was reported to be alive and apparently well 1 year following surgery. With today's refinements in surgical technique and supportive care, it would seem that such early definitive treatment is not only justifiable, but necessary if the salvage rate is to be improved in these people.

SUMMARY

1. Two cases of carcinoma of the colon in individuals less than 20 years old have been presented, with a statistic study of these and 86 other such cases reported in the literature.

2. An increased incidence of "colloid" carcinoma is encountered in this age group and is thought to contribute to the poor prognosis.

3. Reference is made to the treatment of polyposis and ulcerative colitis in youth as possible "premalignant" conditions.

4. The importance of the early recognition and of early and vigorous treatment of carcinoma of the colon in young people is reemphasized.

land for his description of the pathologic material in the case reports.

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RADICAL NECK DISSECTIONS IN THE MANAGEMENT OF HEAD AND NECK CARCINOMA

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The treatment of metastatic cervical nodes overshadows in importance all other considerations in the management of carcinoma of head and neck sites.[6] Radical neck dissection as advocated by Crile,[8] in 1906, remains the standard method of treating cervical nodal metastases from primary malignant lesions of the head and neck.

The extent of the cervical dissection has remained essentially the same since Crile's original report. The block dissection of the cervical nodes and lymph-bearing fascia from the mandible to the clavicle and from the midline of the neck to the anterior border of the trapezius muscle is the classic extent of the operation. Limited or partial neck dissections, usually of the supraomohyoid type, are widely used but these operations leave behind the lower jugular chain where subsequent metastatic involvement may become apparent. The extended retrohyoid dissections have not been proved to be superior to the usual operation.[21]

Much more controversial than the extent of the radical neck dissection is the timing of the operation under certain circumstances. Patients with operable, palpable cervical nodes whose primary malignant head or neck tumor is thought controllable and who have no distant metastases are treated by radical neck dissection in preference to any other mode of treatment.

Patients with intraoral carcinomas without palpable cervical nodes are usually treated by associated radical neck dissection when surgical treatment of their primary tumor enters the neck.

The so-called prophylactic neck dissections remain controversial. These operations are advocated because clinically undetected nodal metastases are removed. A second reason is that there is often difficulty in follow-up examinations on patients whose primary lesions have been treated, and the neck dissection is a better cancer procedure when combined with surgical treatment of the primary.

It has also been pointed out that the mortality

of neck dissection is low (1 per cent) and the comparison of salvage rates in patients having therapeutic neck dissections *versus* those receiving elective neck dissections favors the latter group.[19]

The argument against prophylactic neck dissection is that a large number of unnecessary operations are performed because of patients in whom (1) no cervical metastases will develop; (2) primary tumors will not be controlled; (3) distant spread will occur. (The third group is extremely small in the absence of involved cervical nodes.) In other patients the primary tumor is located at or crosses the midline so that bilateral spread must be anticipated, and the first cervical metastases may appear contralaterally even in unilateral lesions. Finally, the authorities who do not favor prophylactic neck dissection point out that salvage can be achieved when clinical evidence of disease in the neck appears.[19]

MATERIALS

In the light of this controversy over prophylactic neck dissections, our current practice is reviewed in reporting 50 consecutive radical neck dissections in patients with carcinomas of head and neck sites operated upon between 1954 and 1958. This small series of cases was drawn from private general surgical practice and, as such, the distribution of the cases differs from many larger institutional reports.

In our series the age range of the patients was from 18 to 83 years. The average age was 53 years and there were 34 men and 16 women. The younger women patients were largely in the thyroid carcinoma group.

The distribution of the primary sites is given in table 1. In one patient, the primary site was never identified, even at autopsy, where a very careful search for a primary malignant tumor was made. One patient who had previously had squamous carcinomas of the skin of the face was operated upon for presumptive metastatic squamous carcinoma in cervical nodes, and this patient proved to have Boeck's sarcoid.

In the oral and pharyngeal group, there were

TABLE 1

Radical neck dissections 1954–1958

Primary Sites	Cases
Mouth, pharynx or larynx..........	17
Thyroid............................	11
Melanoma.........................	10
Other skin primary site............	6
Salivary gland.....................	4
Primary site not identified.........	1
Nonmalignant (Boeck's sarcoid)....	1
Total......................	50

TABLE 2

Oral, pharyngeal or laryngeal group

	Cases	Initial Therapy	
		Surgery	Irradi- ation
Hypopharynx or extrinsic larynx..................	3	0	3
Gum (alveolar ridge).......	5	5	0
Floor of mouth............	4	1	3
Buccal mucosa............	3	1	2
Tonsillar pillar............	1	0	1
Tongue...................	1	0	1
Total................	17	8	9

16 men and 1 woman. The average age was 63 years and there were 16 squamous carcinomas and 1 adenocarcinoma arising in a minor salivary gland. The initial therapy of the primary tumors of this group is shown in table 2. Seven of the patients had radical neck dissections in continuity with surgical treatment of their primary lesion. It may be noted that the patients with carcinoma of the gum were suspected of having invasion of the underlying bone and were all treated by surgery initially. No 5-year survivors in patients with cancer of the gum treated entirely by irradiation therapy were reported in one large series.[18] Irradiation therapy had been carried out previously for the majority of the other primary lesions.

Of the patients with primary intraoral lesions, 40 per cent had been inveterate intraoral snuff users for more than 20 years.

Clinically, the cervical nodes were felt to be involved in 14 of the 17 patients in the oral and pharyngeal group and these nodes were found on pathologic examination of the operative specimen to be involved in 13 patients. The nodes of 3 patients were felt to be negative, but radical neck dissections were performed in these cases because surgical treatment of the primary entered the neck; in 2 of these patients involved nodes were found.

The survival figures in these patients are for less than 5 years; no valid conclusions can be drawn from this small series, but the 3 patients whose cervical nodes were not palpable are living and well 2 or more years after radical neck dissection.

During the 5 years, 1954 through 1958, 370 thyroidectomies were performed by our surgical group (table 3); 22 carcinomas of the thyroid were found in this same period. There were 15 papillary adenocarcinomas of the thyroid and 4 of these were of the occult sclerosing variant. The types and the patients having associated radical neck dissections are presented in table 3. One patient had bilateral cervical nodal metastases from a papillary adenocarcinoma of the thyroid, and he was treated by total thyroidectomy and staged bilateral radical neck dissection preserving the internal jugular vein on the second side. This patient had minimal facial edema.

There were 7 women and 4 men with thyroid carcinomas who had radical neck dissections. The average age of this group was 36 years. The pre-

TABLE 3

1954–1958

	Total Number
Thyroidectomies....................	370
Thyroid carcinomas................	22

Pathologic Types	Cases	Associated Radical Neck Dissection
Papillary (occult sclerosing variant, 4)................	15*	8*
Follicular....................	4	3
Adenocarcinoma (angioinvasive).....................	1	
Undifferentiated.............	2	
Total...................	22	11

* One bilateral.

senting symptom was thyroid enlargement in 7 cases and cervical nodal enlargement in 4 cases.

The indications for radical neck dissection were palpable cervical nodes, in 5 patients, and absence of an encapsulated primary tumor, in 6 patients. On pathologic examination of the surgical specimens, nodes were found to be involved in 5 of the 11 patients.

DISCUSSION

Despite the excellent results reported with surgical approach limited to portions of the cervical nodes in papillary thyroid cancer,[3] we have been impressed with the high percentage of involved nodes found on careful dissection of block specimens,[13] and for this reason we have performed radical neck dissections in this group except for the localized primary tumors. The transformation of papillary adenocarcinomas of the thyroid to anaplastic tumors has been reported in 14 cases.[9, 13] The anaplastic tumors are practically all inoperable when first seen.

In this small series one young woman, 18 years of age, had irradiation to the neck for tonsillary enlargement 8 years before admission for papillary carcinoma of the thyroid with cervical metastases. Recently, 121 patients with thyroid cancer who had previous x-ray therapy in early childhood to the thymus or head and neck areas for benign conditions were reported.[23] Of 357 children with reported thyroid carcinomas, approximately one-third had received prior irradiation to the pharynx, neck or chest for nonmalignant conditions.[24] It seems clear that children should be protected from ionizing radiation in the treatment of benign conditions in this area to diminish the possibility of later developing thyroid carcinoma.

In the 10 patients with malignant melanoma of head and neck sites, the cervical nodes were thought to contain metastatic tumor in 7 instances, and all but 1 of these were confirmed on pathologic examination of the surgical specimens. Two patients who had declined radical neck dissection prophylactically returned after 1 year with involved nodes. Radical neck dissections were then performed, but both patients died less than 1 year after the second operation. We feel that prophylactic neck dissection has a very definite role in the management of melanoma of the head and neck.

Patients with carcinomas of the tail of the parotid gland and of the submaxillary or sub-

TABLE 4
Complications

Postoperative hemorrhage requiring tracheostomy................	1
Wound slough, partial.............	5
Parotid fistula.....................	1
External auditory canal infection...	1
Operative mortality................	0

lingual salivary glands require radical neck dissection.in continuity with excision of the primary lesion. Copeland[10] reported that cervical nodal metastases averaged 32 per cent in uncontrolled carcinomas of the parotid late in the clinical course of the disease. The natural history of the malignant parotid neoplasms shows considerable individual variation as regards local recurrence and regional lymph node involvement.

The complications encountered in this series are listed in table 4. Tracheostomy on an emergency basis was required in one instance. Tracheostomy is routinely performed in any case in which the mandible is sectioned, or in any case in which there has been prior intensive radiation therapy, or in a bilateral radical neck dissection.

Partial wound sloughs were encountered in 5 cases, but no secondary grafting procedures were required in this group. The platysma is routinely included in the skin flaps unless attachments of involved nodes require excision of portions of the platysma or skin.

The parotid fistula and external auditory canal infection cleared after several weeks.

Routine identification of the marginal mandibular division of the facial nerve is important in avoiding facial disfigurement. This division of the facial nerve is spared unless removal of the mandible is required. The impairment incident to sacrifice of the spinal accessory nerve is accepted in practically all cases since the spinal accessory nerve is in intimate contact with the most frequently involved cervical node, the subdigastric node of the upper jugular chain. In papillary and follicular thyroid carcinoma, the spinal accessory nerve is sometimes spared if there is no indication of involvement in the upper jugular chain.

In this small series there was no operative mortality. The morbidity is greater in those cases in which there is surgical treatment of the primary oral tumor in continuity with radical neck dissection.

The extended operations are now resulting in

an improved 5-year salvage rate as compared with those before 1955 when the 5-year survival rate was 15 and 30 per cent in carcinomas of most head and neck sites with cervical metastases except for squamous carcinomas of the skin and low grade thyroid carcinomas.[10]

CONCLUSIONS

1. A recent series of 50 consecutive radical neck dissections for metastatic carcinoma from primary head and neck sites is presented.

2. The usual block dissection is felt to be superior to more limited forms of neck dissection and is well tolerated.

3. In the absence of palpable nodes, radical neck dissections are employed in malignant melanoma of the head and neck, and in cases where surgical treatment of the primary intraoral tumor enters the neck.

4. Primary head and neck malignant tumors with great propensity to early unilateral cervical metastases are often best treated by associated radical neck dissection, in the absence of suspicious cervical node enlargement.

5. The case of a young person having radiation therapy to the neck in childhood for a benign condition followed by carcinoma of the thyroid with cervical metastases is reported. A total of 121 cases of this type have been previously reported.

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"CONTRA COUP" INJURY TO THE LIVER AND CYSTIC DUCT:
A CASE REPORT

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Injury to the liver by the application of blunt force to the abdominal wall is not uncommon and, fortunately, is usually not severe. Injury to the biliary drainage system by blunt abdominal trauma is rare, with Mason and associates[2] estimating, after an extensive review of the literature, that less than 100 cases had been reported. The authors have recently treated a patient who received, from a blow across the left scapula, extensive hemorrhage into the right lobe of the liver and amputation of the cystic duct from the common duct.

CASE REPORT

A 44-year-old colored man was brought *via* ambulance to the emergency room of the L. Richardson Memorial Hospital. He complained of pain in the region of the left scapula and stated that he had been struck there by a swinging steel beam a short time before. The impact was such that it had knocked him to his knees but shortly he stood up by himself and walked to the first-aid station.

Examination on admission showed that he was orientated but in mild shock with a blood pressure of 80/40 and his skin was moist and cool. Because of the chest pain, he was breathing with some little difficulty. There were abrasions and tenderness over the left scapula. All extremities moved normally and reflexes were physiologic. Breath sounds were good bilaterally. The abdomen was soft and relaxed, the genitalia normal. Normal saline was begun intravenously while awaiting cross matching of blood for transfusion. Meanwhile, x-ray examination of the chest and spine showed fractures of the blade of the left scapula and the left 6th and 7th ribs just lateral to the necks of the ribs. The laboratory examination results were as follows: urinalysis, specific gravity 1.023, albumin 1+, 50 RBC per high power field, 15 to 20 WBC per high power field; hemogram, 12 gm. of hemoglobin, 15,500 WBC per cu. mm. with 80 per cent polymorphonuclear leukocytes and 20 per cent lymphocytes.

A transfusion of 500 cc. of whole blood was given, and within the hour his blood pressure rose to 120/80, and he appeared much improved. He still complained only of diffuse pain across the left shoulder blade. He rested well that night. The following morning his blood pressure was up to 180/120, and breathing was more labored. Abnormalities noted now included the abrasions across the left posterior thorax, plus tenderness in the left loin and signs of pulmonary consolidation at the left lung base (dull percussion note, diminished breath sounds, rales). There were rales present on the right, but the percussion note was resonant. The abdomen was slightly distended, but soft. To deep pressure, there was a little tenderness high in the upper left quadrant of the abdomen. To auscultation, peristalsis was quite active over the entire abdomen, but the patient had not passed any flatus since entering the hospital.

X-ray examination of the chest at this time showed considerable diffuse infiltration throughout the left lung and almost solid consolidation of the lower part of the lung. X-ray examination of the abdomen showed diffuse, mild, small and large bowel gaseous distention. It was postulated that he had a crush injury of the left lung with diffuse hemorrhagic infiltration, and undoubtedly a contusion of the left kidney as evidenced by the loin tenderness and hematuria. The abdominal distention was believed to be secondary to ileus resulting from the known injuries to the ribs and kidney. Oxygen administration *via* tent was begun. Since he was unable to cough, or would not cough, it was felt that bronchoscopy was indicated and that possibly a tracheotomy might become necessary. (The location of the rib fractures precluded local nerve block anesthesia for relief of pain.) Bronchoscopy was performed under local topical anesthesia with a moderate amount of thick bloody fluid being obtained. He immediately breathed easier and requested to be let out of the oxygen tent. His condition seemed good.

The following morning he was better, and was coughing without any difficulty. At this time there was only an occasional red blood cell in the urine. Subcutaneous emphysema of the left lateral and posterior chest wall was noted for the first time, but his breath sounds were improved and x-ray examination did not reveal any evidence of a pneumothorax. Some time during the 3rd hospital day he began to pass flatus, but remained dis-

tended. Gastric dilation was suspected; a naso-gastric tube was passed, resulting in the recovery of about 1000 cc. of fluid and a large amount of air, with complete alleviation of the abdominal distention. The tube was left in place and he was maintained on intravenous fluids, in an effort to keep distention to a minimum. During the night he removed the stomach tube and the following morning he was again distended but there was absolutely no rigidity or tenderness to palpation of the abdomen. Prostigmine was given to encourage the passage of flatus but unfortunately the medication caused marked sweating, a fall in blood pressure and nausea, thus precluding its use.

On the 5th hospital day he was still distended and it was speculated that he might have had, in some unaccountable manner, an injury to his intestine. Chloromycetin was given intravenously and he was put back in an oxygen tent; the former in case he did have an injury to the intestine (he had been on penicillin and streptomycin since admission); the latter in an effort to minimize the distention. All-in-all, the patient felt fairly well, and both he and his physicians believed that there was improvement.

On the 6th hospital day he had several loose stools (normal brown color, negative for blood) without reducing the amount of distention. His lungs sounded good, and a chest x-ray showed a good deal of clearing of the pulmonary consolidation. The next day he continued to pass flatus, but without lessening the degree of distention. Gastric aspiration was nonrewarding, and the patient refused to leave a tube in place for more than 1 hour. On the morning of the 8th hospital day, for the first time there was dullness in the lower abdomen, with resonance above. The abdomen remained soft and nontender but now it was absolutely silent to auscultation. His hemoglobin was found to have dropped 3 gm., from 12 to 9 gm., in the past 2 days. Since the only abdominal tenderness he had had at any time had been in the left upper quadrant, it was thought that the most likely diagnosis was rupture of the spleen, with delayed hemorrhage. Exploratory laparotomy seemed mandatory.

After giving 1000 cc. of whole blood intravenously, laparotomy was performed under general anesthesia. An upper left rectus incision was utilized. As the peritoneum was opened there was a deluge of greenish fluid; aspiration yielded 6000 cc. of this fluid. Exploration revealed the spleen to be small and intact. There was a fracture (2 cm. deep) across the dome of the right lobe of the liver; bile was oozing from this raw surface. The pancreas was enlarged, and the gastrohepatic ligament quite edematous. The gall bladder was collapsed. The bowel was empty, with

no evidence of injury. It was believed that all of the intraperitoneal bile had drained from the ruptured area of the liver. Since suture of this 8-day-old injury of the liver was obviously impossible, the area was drained to the outside with multiple catheters, with the thought that the bile could subsequently be fed back through a gastric tube. The wound was closed without any untoward incident and the patient transferred to his room in a reactive state. A few minutes later he suddenly ceased to breath and shortly died.

Autopsy examination (courtesy of H. C. Lennon, M.D., pathologist) was performed a short time after death. Abnormalities included 300 cc. of dark greenish fluid in the abdominal cavity and approximately 200 cc. of blood tinged fluid in the left pleural cavity. The left 6th and 7th ribs were fractured as noted clinically and, in addition, the left 8th rib was found to be fractured at about the midaxillary line. The pericardial cavity contained a little blood tinged fluid, but there was no evidence of any myocardial contusion. The lower lobe of the left lung was completely atelectatic; the lower lobe of the right lung was partially atelectatic. The liver showed a long (15 cm.) fracture across the dome of the right lobe as previously described. On section there was evidence of extensive hemorrhage beneath this fracture and, in addition, in the midportion of the liver there was an extremely large softened hemorrhagic necrotic area measuring 10 to 12 cm. in diameter. The gall bladder was firmly attached to the undersurface of the liver, but no attachment between the cystic duct and the common duct could be found. The hepatic and common ducts were dissected out, and a small opening was located in the common duct where the cystic duct had joined it.

The spleen was small, perfectly normal. There was no abnormality of the adrenals. The pancreas was rather firm with a few small areas of fatty necrosis but no hemorrhage. Each kidney was slightly enlarged with microscopic examination showing only cloudy swelling. The esophagus and stomach were normal, whereas the small intestine was dilated with a dark, watery fluid. The large bowel and rectum were normal. Death was attributed to a combination of factors; chiefly, rupture of the liver with massive intrahepatic hemorrhage and necrosis with resultant hepatic insufficiency, plus biliary peritonitis and atelectasis of the lungs.

DISCUSSION

The mode of injury to the liver and cystic duct in this case is difficult to reconstruct. In other reported cases of injury to the biliary tract due to blunt abdominal trauma, the force has been applied, almost invariably, directly to the upper

quadrant of the abdomen. Injury to the underlying viscera thus may occur (1) directly from the blow, (2) by tearing action, when the less fixed liver moves away from the more fixed pancreas, or (3) by a pinching action between the posterior abdominal wall and the applied force anteriorly. None of these methods would seem to apply in the case being reported. This man was struck on the left posterior chest wall, at the 6th-7th-8th rib level. The liver and bile ducts seemingly must have been injured owing to their inertia, in that the body shell was set in motion rapidly, with the internal organs starting in motion later, but continuing in motion after motion of the body shell stopped. This would result in the liver and gall bladder striking the anterior ribs, perhaps the rather sharp costal margin, with considerable force. Such an injury of the brain is seen not infrequently and is known as a "contra coup" injury. Another possibility exists in that when the man was struck down, his knee might have been driven against the upper abdomen to inflict the known injury. However, this surely would have also injured the anterior abdominal wall to such a degree that some tenderness, and even spasm, should have resulted. Obviously, it is impossible to confirm the mental image of the *modus operandi*.

The diagnosis of an injury that ruptures the biliary tree may be difficult, even with a history of a blow to the upper abdomen. In the typical case, there is nothing significant on the initial examination to suggest rupture of the biliary tract, but in a few days jaundice, abdominal distention and acholic stools are noted. Mason and associates[2] note that jaundice is a constant finding in rupture of a bile duct, but rare in rupture of the liver. In the patient under discussion, clinical jaundice did not occur, and his stools remained brown, although they were scanty. The recognition of peritoneal fluid was delayed by the concurrent adynamic ileus. The delayed drop in hemoglobin served to focus attention on the spleen, particularly since the blow was received on the left posterior chest wall, fracturing ribs 6, 7 and 8, as it did. Even at exploration the diagnosis was missed, since the biliary peritoneal fluid was attributed to leakage from the extensive fracture across the dome of the liver (rupture of the biliary tree was not suspected until the autopsy was performed).

Treatment of an injury to the liver is usually limited to stopping hemorrhage and removal of devitalized fragments. In the ordinary type of injury to the liver, as demonstrated by the fracture of the dome, wherein bleeding has ceased at the time of operation, only drainage is indicated. In tears of the liver that are actively bleeding, control of same by packing (gauze, or preferably an absorbable packing) or suturing, with adequate drainage, is indicated. In subcapsular liver injuries, which incidently, as pointed out by Sparkman and Fogleman,[3] carry the highest mortality rate of any type of liver injury, there is no treatment indicated, other than general supportive.

The treatment of rupture of the biliary tree is simple. In the majority of the cases the rupture is in the form of a rent in the duct, rather than a complete division. Thus adequate drainage of the escaping bile, with refeeding of same to prevent inanition, will usually suffice to effect a cure. Primary suture of the defect is almost impossible due to difficulty in locating the defect and, once located, in suturing the edematous structures. (However, primary suture of a common duct that was completely divided by blunt abdominal trauma has been reported by Donald and Donald.[1]) If after prolonged drainage there is no indication as to cessation of the flow, a secondary repair is in order. Usually, a stricture of the bile duct distal to the tear must occur to prevent satisfactory healing. In the case being reported the patient's demise from his severe liver damage precluded other than initial treatment of the biliary duct injury.

SUMMARY

A case of a fatal liver injury, with concurrent traumatic amputation of the cystic duct from the common bile duct, is reported. The damage was notable in that it resulted from a blow across the left mid-posterior chest, and represents a "contra coup" type of injury.

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CHYLOUS ASCITES IN CHILDHOOD

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Despite nearly 300 years of struggle with the problem of intraabdominal lymph fistulas, the physician is still often unable to control chylous collections within the abdomen. This is in contrast to the recent successful treatment of intrathoracic collections of chyle, in which ligation of the main thoracic duct has produced excellent results in controlling this complication of thoracic surgery.[30] The efforts of the surgeon to reverse the production of intraabdominal chyle with dietary measures, paracentesis, and perhaps ill conceived decompressive operations, would suggest that there is valid reason for reexamination of this distressing clinical syndrome.

The present paper offers no new concepts of therapy, but the clinical situation in which chronic chylous ascites presented itself to the authors was so unusual that the following report was felt justified. The etiology of the ascites in the patient reported below is a secondary facet of this case, which in itself probably deserves attention. The presence of a ruptured appendix with its associated chronic pelvic abscess of 2½ years' duration, presenting clinically as chylous ascites, must certainly be unusual. It might also serve to emphasize that chronic chylous ascites should not be approached with undue pessimism, even in the face of previous unproductive surgical exploration.

CASE REPORT

M. T., a 5-year-old colored boy, was admitted to the Brewster Hospital on June 3, 1958, with a history of proven chylous ascites. At the age of 20 months, some 2½ years before the present admission, the parents stated that the child had had an episode of fever with apparent abdominal pain and short lived diarrhea. The child was unattended by a physician at that time and apparently recovered from this acute illness without creating any particular concern to the parents. It was only with prolonged and careful questioning that this history of minor illness could be obtained. However, at the age of 22 months, some 2 months after the illness described above, edema of the penis and scrotum was noted. This was slowly progressive and over the ensuing months swelling of the abdomen had begun. In January

1956 the child, otherwise apparently active although somewhat undernourished and anorexic, developed bilateral edema of his legs and a further enlargement of the girth of his abdomen. He was admitted to an Air Force Hospital in Texas where extensive medical work-up revealed no evidence of renal, hepatic, or malignant disease as etiology of the ascites. Abdominal paracentesis at that time produced a large quantity of milky, sterile abdominal fluid which was diagnosed in the laboratory as chyle. Free fat was stained in this fluid and its protein content was found to be in the neighborhood of 2 gm. per 100 ml. on several occasions. Further study was carried out at another military hospital, after which the child was lost to follow-up for 1 year. In March 1957 he was readmitted with progressive symptoms, to an Air Force Hospital, and underwent exploratory laparotomy on March 1, 1957. The operative note indicated that the surgeon recognized a tremendous quantity of chylous ascites upon opening the abdomen and, again, chemical and bacteriologic studies revealed the typical characteristics of chyle. The child developed an anesthetic complication during the early phases of this laparotomy and the abdomen was closed with no apparent extensive exploration carried out. He recovered from surgery and was treated medically on a dietary regimen. His symptoms continued until 2 years later, when on May 20, 1958, the patient was admitted to the United States Naval Hospital, Jacksonville. Abdominal paracentesis again yielded 1000 cc. of slimy, cloudy, ascitic fluid. This again was sterile to culture and showed free fat on examination in the laboratory. The serologic test for syphilis was negative; PPD No. 2 was negative on three occasions; thymol turbidity, 0.8 units; total serum protein, 2.8 gm. per 100 ml.; A/G ratio, 1.7 to 1.1; urea nitrogen, 9 mg. per 100 ml.; serum chloride, 106 mEq./L.; prothrombin time, 17 seconds or 75 per cent of control. Many urinalyses were normal. After prolonged dietary therapy, the serum proteins rose to 3.7 gm. per 100 ml. with an A/G ratio of 2.5 to 1.2.

The child was seen to be marasmic in appearance with a grossly swollen abdomen and left leg. The scrotum and penis were moderately swollen (fig. 1). The child's mental status was quite acute, however; he was cheerful, active and intelligent. Abdominal examination showed a right vertical
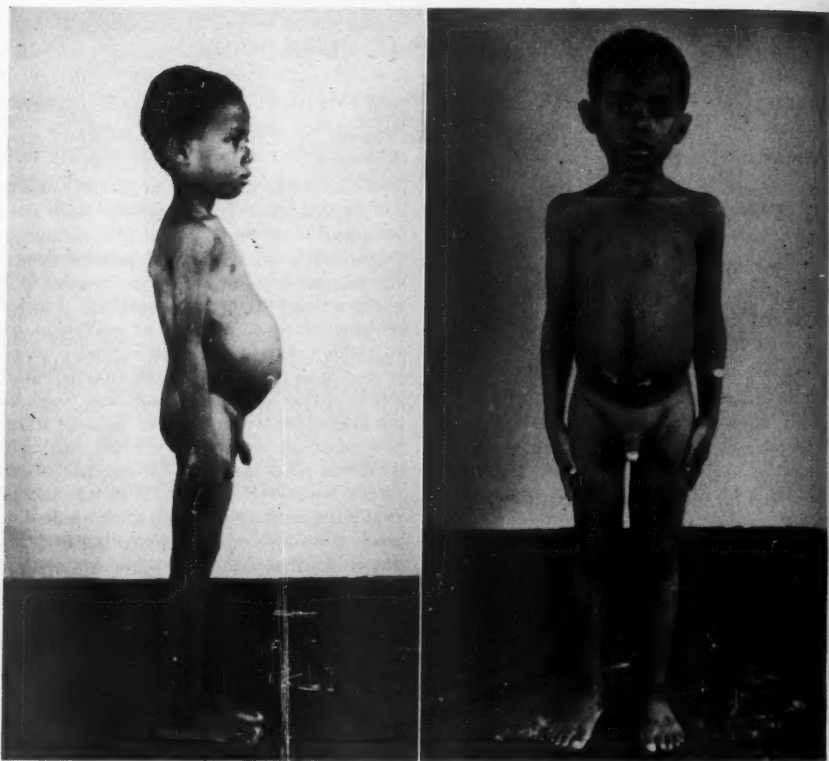
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Fig. 1. Preoperative appearance of child with abdominal protrusion, edema of penis and general evidences of weight loss. Note asymmetry of leg edema.

paramedian scar which was well healed. The abdomen was diffusely rounded and obviously contained a large quantity of fluid. By ballotting the fluid, the liver edge could barely be felt in the right upper quadrant. No other abdominal masses were palpable. Rectal examination was negative. The left leg showed a 3+ pitting edema throughout which extended from toes to groin. The right leg was swollen, but not nearly so markedly as the left leg. There was a small degree of postsacral edema. Neurologic examination was negative. Abdominal x-ray showed diffuse clouding of the abdominal shadows secondary to the fluid collection. There was an extremely dense, square, calcific shadow that persisted in the right lower quadrant and was highly suggestive of a tooth. This was felt probably to represent an intraabdominal teratoid tumor, although no mass could be felt (fig. 2).

On June 6, 1958, abdominal exploration was carried out through the old paramedian scar. There was a large quantity of typical chylous fluid within the abdomen and the whole of the serosal surfaces of the intestinal tract were leathery, gray-white, with obvious marked dilation of the lacteals (fig. 3). Several large mesenteric lymph nodes were present throughout the base of the small intestinal mesentery. A loop of distal ileum was densely adhesed in the right pelvis where a firm mass lay in midpelvis, measuring about 4 by 5 in. in diameter. This was overlaid by several adherent loops of ileum and the operator originally thought that the mass probably represented a presacral teratoma. However, upon freeing the bowel from this mass, during which maneuver it was necessary to resect a portion of ileum, a lemon sized intraabdominal abscess which contained thick, yellowish pus was entered. The abscess wall was thickened and was excised as a discrete entity. Within the abscess cavity lay the remnants of a ruptured appendix, within which was a calcified fecalith. After removing the main mass, we directed our

attention to the extensive pelvic scarring in the retroperitoneal tissues. The left iliac vein was densely bound in overlying scar tissue which was excised insofar as possible. This freed to a considerable degree the common iliac vein. A careful search of the retroperitoneal area by inspection and dissection was completed to rule out the presence of any further obstructing mechanism. No evidence of discrete chyle leakage could be found. The whole of the retroperitoneal area, however, was diffusely thickened and edematous, secondary to the chronic protein loss and the long standing lymphatic obstruction. An end-to-end ileoileostomy was completed and the patient recovered satisfactorily from the operative procedure (fig. 4).

The postoperative course showed a dramatic diminution in the size of the left leg and the abdominal swelling. His diet was continued as a high protein, low fat regimen and the child gained weight and strength steadily. At the time of discharge his serum proteins were 4.5 gm. per 100 ml. Bacteriologic studies of the contents of the pelvic abscess revealed a pure culture of *Escherichia coli.*

The child's subsequent course for 5 months was apparently without complication until, on October 22, 1958, he was returned to the Naval Hospital by his parents, with the complaint of a sudden generalized convulsion, lasting for several minutes and ending in a Jacksonian type

FIG. 2. Preoperative lateral abdominal x-ray showing free ascites and calcific density in lower quadrant, felt to be possible tooth in teratoma before operation.

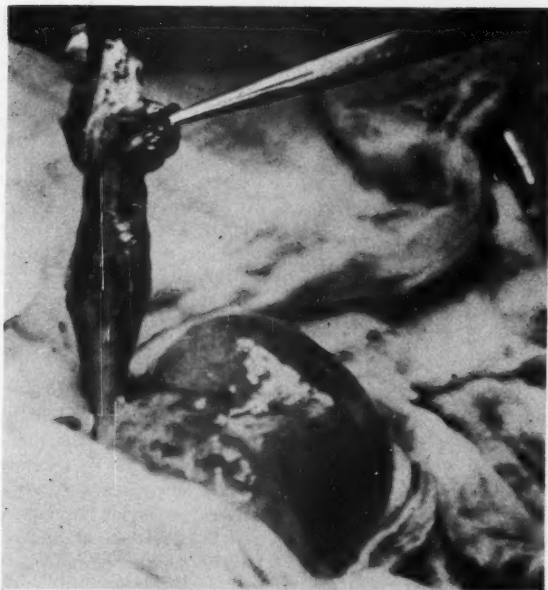FIG. 3. Operative exposure of a 2½-year-old appendiceal abscess

FIG. 4. Operative exposure of old ruptured appendix. The tip containing calcified fecalith lay in the chronic abscess.

right sided convulsive movement. Examination on admission to that hospital showed the child to be markedly obtunded mentally, with a high pitched cerebral cry, fever of 100.6° and a white blood cell count of 6000. The differential was normal. Lumbar puncture showed an opening pressure of 200 mm. of spinal fluid; closing pressure, 100 mm. The fluid was clear; protein, 23 mg. per 100 ml.; sugar, 85 mg. per 100 ml.; chlorides, 130 mEq./L.; microscopic, 5 lymphocytes. The patient's fasting blood sugar was 96 mg. per 100 ml.; blood urea nitrogen, 7 mg. per 100 ml.; and nonprotein nitrogen, 39 mg. per 100 ml. The remainder of his serologic studies of pertinence indicated a rise in the total protein to 5.4 gm.; globulin, 3.4 gm.; with normal ratios of the alpha, beta and gamma fractions. Neurologic examination was entirely negative except for the gross aberrancy in the sensorium, the child having become dramatically reverted from an acute, intelligent, friendly individual to a most distressingly obtunded child who had shown almost complete loss of affect. An electroencephalogram on October 23, 1958, showed generalized wave abnormalities without specific localization. The child was transferred to the neurosurgical service under the care of Dr. C. A. Bird, where ventriculography showed no evidence of an intracranial space occupying mass. After further neurologic study it was felt

that the child had Schilder's disease. His subsequent development of bilateral deafness and blindness would confirm this. It is not felt that the degenerative brain disease is connected with the original illness.

At the time of this final admission, the child's abdomen remained of normal contour on a low fat diet.

HISTORICAL

In 1694 Morton[32] described the first reported case of an infant with apparent chylous ascites. He deduced that the fluid collection within the abdomen of an otherwise hungry child represented the loss of nutritional elements from the lymphatics of the abdomen. This was confirmed by paracentesis and a clinical note stated: "But at the very beginning of the Fever his belly began to be distended with a dropsical swelling, which increased strongly every day; his Cough and shortness of Breath at the same time growing worse; All which symptoms were at length accompanied by Atrophy of the Parts, even to the degree of a Marasmus. But yet when his body was a perfect Skeleton, and the Dropsie at a high Tide (which was very remarkable) he had a brisk and healthful look, and a lovely counte-

nance, without the least Tincture of a yellowness, and a good or rather greedy Appetite, and that to the very day he dyed. From whence I did rightly conjecture, and always told his Friends, as my opinion, that his Dropsie was truly chylous, caused by the chyle flowing into the cavity of the Belly by lacteal vessels upon some rupture that had been made in them; which appeared very plainly from the Event."

It is of real interest that this clinical diagnosis of chylous ascites has been made on so few occasions before abdominal exploration, since the astute deductions of this English physician. The literature is replete with reports of chylous ascites since Morton's original paper.[4, 6, 15, 20, 29, 40, 43] Excellent reviews of the clinical and pathologic nature of chylous ascites have been frequent in foreign and American literature, but articles by Hoffman[19] and Nix and associates[33] probably represent the classic clinical reviews.

Chylous ascites in infancy and childhood has been an infrequently reported clinical syndrome.[17, 21, 25, 26, 42] In 1952 Kessell[23] reported 31 collected cases of chylous ascites in children, and in 1953 Blood and Fairchild[5] recorded 50 collected cases occurring in children under 15 years of age. A recent article by Whittlesey,[46] in which 5 further cases of chylous ascites in children were added to the literature, is of particular interest in that his first case is the only other example in the literature of gangrenous appendicitis being associated with chylous ascites. In this instance he describes a 5-week-old male who was operated on for an acute abdomen, during which exploration he was found to have a small, avascular, gangrenous appendix wrapped about the ileum with a considerable collection of chyle within the abdomen. This infant was reoperated on 5 days later for intestinal obstruction, at which time the chyle was nearly absent from the peritoneal cavity. A situation in which *chronic* chylous ascites has occurred in association with gangrenous appendicitis and abscess has not been found in a rather careful search of the literature. The great majority of case reports have shown no specific etiologic agent for the development of chylous ascites in the child. Many, however, have been related to widespread intestinal tuberculosis, 2 cases secondary to rupture of a mesenteric chylous cyst, some to advanced intraabdominal malignancy with invasion of the cisterna chyli, a rare case from mesenteric lymphadenitis, and even rarer cases from associated small intestinal ob-

struction.[1, 9, 10, 14, 41] Very unusual reports of mechanisms of production of chylous ascites in the adult have included strangulated scrotal hernia, term pregnancy, cardiomegaly, pancreatic cyst, stone in the receptaculum chyli, and other weird lesions.[7, 11, 13, 18, 36] These, however, have not appeared to be of any diagnostic significance in the childhood age groups. Presumptive congenital chylous ascites has been reported in 2 children by Kessel[23] and Kerr,[22] the youngest of these infants being 16 days old. The etiologic agent was never found.

An analysis of pediatric chylous ascites would indicate that 40 per cent can be shown to have some distinct etiology at laparotomy or autopsy. Of those infants subjected to surgery, 27 per cent have died eventually of their disease. Of infants treated by expectant paracentesis, 22 per cent have died.[17] It is obvious that these figures are weighted and dependent entirely on whether the etiologic agent has been surgically or medically correctable.

It would certainly appear that thorough exploration should be a part of the diagnostic work-up in an infant with chronic chylous ascites in the real hope of finding a correctable lesion. This might best be deferred until a short trial of paracentesis had proved unsuccessful.

Of the surgical procedures attempted, excisional surgery of obstructing masses has proved the most successful. The saphenoperitoneal shunts of Talma[39] and Ruotte[34] have been surprisingly effective in scattered reports[8, 31, 45] but one wonders whether the anastomosis between vein and general peritoneal cavity actually functioned, or the ascites resolved by natural remission. Other attempts to shunt chyle into surgically created subcutaneous pockets[21] or the use of glass[12] or vitallium[37] buttons to direct chyle into extraabdominal tissues have proved discouraging.

PATHOLOGIC PHYSIOLOGY

Anatomically, the course of the major channels of the chyle systems has been well described. Recent interest in thoracic duct ligation for chylothorax has produced several excellent anatomic studies which indicate that the main thoracic duct may have many variations in its anatomic location, but ordinarily extends from the second lumbar vertebra to the junction of the left internal jugular and subclavian veins. Its course along the spinal column is posterior and

somewhat to the right of the aorta. It is usually quite easily found just above the diaphragm as a visible, thin walled lymphatic channel 2 to 3 mm. in diameter and lends itself, in this position, to surgical manipulation. The origins of the thoracic duct generally are four in nature, being formed from the union of three lumbar nodal collecting ducts and a single unpaired intestinal trunk which drains the digestive tract. The dilation of these confluent ducts at the level of the second lumbar vertebra represents the cysterna chyli into which all collecting ducts from the abdominal cavity empty. The embryologic studies of Sabin[35] and, later, the dissections by Lee[27] showed that there are numerous communications between the lymphatics of the thorax and the intercostal veins or other branches of the azygous system, most of which empty *via* the right jugular or innominate veins as the right thoracic duct. The probability of extraperitoneal lymphaticovenous communications has been emphasized by Blalock and associates.[3]

Chyle represents a specialized form of lymphatic fluid only insofar as it carries the intestinal products of fat digestion in the gastrointestinal tract. The characteristic opalescent or milky appearance is readily recognizable by the observer. Chyle is sterile on culture, shows great numbers of large fat globules, rare red blood cells, a few polymorphonuclear leukocytes, and some lymphocytes. Sudan III will produce a positive fat stain. On treatment with ether, the fluid is extracted into a creamy layer which rises to the top of the test tube. The protein content of chyle is ordinarily less than one-half that of the patient's serum proteins. The fat content is always considerably higher than serum fats. The old discussions in the literature[4] as to classification of chyle into chyliform, true chyle, and pseudochyle are not germane to the present discussion and should create no confusion when the above criteria of chyle constitution are followed.

The clinical course of a patient with chylous ascites is difficult to understand when considered in the light of what little is known about the chyle system's basic physiology. Attempts to produce chylous ascites of a chronic nature in the experimental laboratory have been fraught with great difficulty. Blalock's group[2, 3] was able to produce total lymphatic blockage in only 3 dogs of over 50 animals in which this was attempted. Their approach was systematic and thorough, consisting of combined operative procedures which obstructed the thoracic duct, the right thoracic duct, cysterna chyli and the distal mesenteric lymphatics, but with little success in what should be a method producing widespread lymphatic blockage.

Why then, in the clinical situation, does a relatively discrete lesion produce chronic chylous ascites?

The experimental attempts of Blalock and others to create chronic chylous collection within the abdomen has emphasized the probability that collateral lymphatic circulation is widespread throughout the abdominal cavity, and it has certainly been demonstrated to be rather diffuse within the thorax. If the lymphaticovenous communications exist to such a degree that experimental obstruction does not produce consistent results, why then should a disease process so often completely or nearly completely obstruct the whole of the abdominal lymphatic system?

It is well known that chronic chylous ascites produces a profound nutritional deficit with depression of the serum proteins, continuing loss of serum lipids and a generally marasmic terminal state. However, Little and associates[28] reintroduced huge quantities of aspirated chyle into a 17-year-old girl by the intravenous route over a period of several months, apparently returning a significant majority of the lost chyle to the venous system, and yet the patient showed essentially no beneficial effect. This would suggest that the peritoneal surfaces, perhaps the parietal peritoneum, can resorb chyle at a rate which will allow a certain nutritional maintenance, until the balance of chyle leakage and chyle absorption has been overburdened. In the author's patient, the gross appearance of the thickened, leathery, serosa of the intestinal tract and of the parietal peritoneum suggested that the absorptive power of these membranes must certainly be drastically reduced. It would almost suggest that free chyle, outside the bounds of its normal channels, acts as a chemical irritant and yet there have been no irritant enzymes demonstrated within chyle save for a low degree of diastatic activity.[19] In cases of acute chylous ascites, many patients have had severe abdominal pain with rigidity and rebound, even suggesting the presence of a perforated ulcer or acute cholecystitis. This would lend credence to the probability that chyle, much like blood, is an irritant to the peritoneum when this membrane is bathed acutely with considerable quantities of the substance. However, ab-

dominal pain in chronic chylous ascites is not a prominent symptom, and in fact most patients seem quite comfortable save for complaints related to the distention of the abdominal wall.

Another factor of physiologic interest is the relationship of intraabdominal or intestinal lymphatics to the lymphatics of the extremities. In the child reported above, bilateral leg edema, most marked on the left, was a prominent feature of the clinical picture. After excision of the pelvic abscess and presumptive release of some of the lymphatic obstruction within the abdomen, the edema of the legs disappeared rather dramatically. This loss of edematous fluid within the leg was so rapid, in fact, that it could hardly have been related to the much slower rise in serum proteins. Whether the restricting scar over the left common iliac vein was the major source of stasis within the leg is conjectural in view of the fact that the right leg was enlarged also. Lee's[2] early studies indicated that one could ligate the thoracic duct within the chest without producing chylous ascites or any significant abnormality of the lymphatic system below the level of the diaphragm, save for a temporary dilation of the lymphatics before collateral channels were opened. Blalock ligated the superior vena cava in animals and produced chronic chylothorax in about 50 per cent of the experimental specimens.[2] Here again there was no production of significant chylous ascites. The expanding clinical experience with ligation of the thoracic duct above the diaphragm for control of traumatic chylothorax would again suggest that the main thoracic duct can be obstructed with relative impunity. However, the author has seen a very provocative development of bilateral lymphedema of the lower extremities in a young male, who underwent thoracic duct ligation for control of chronic chylothorax. This young patient, now aged 10, was operated on by the author in 1955 for pure pulmonic stenosis. Subsequent to the transventricular valvotomy, the patient developed chronic chylothorax which was treated conservatively for nearly 1 year by some 70 consecutive thoracenteses. When he failed to respond to this therapy, open exploration of the left chest was carried out, and supradiaphragmatic ligation of the thoracic duct with pleural poudrage produced a complete clearing of the persistent chylothorax. However, of pertinence to the present discussion, this patient, about 1 year following the ligation of his main thoracic duct, showed a slowly progressive,

indolent enlargement of both lower extremities which has now developed into what one would be forced to call lymphedema praecox, had the prior history not been known. One is forced to reflect on the possible relationship of obstructing the main thoracic duct, to the present development of lymphedematous change in the legs. Supporting the possibility of a relationship in this regard is the work of Servelle and Deysson,[35] who have regularly demonstrated by roentgen dye methods the intercommunication of intestinal lymphatics with dilated lymphatics of the leg in patients with elephantiasis. They have, in fact, actually aspirated chyle from the sole of the foot in several patients with elephantiasis. Chemical analysis of the aspirated chyle from these legs show with little question that the fluid is true chyle and not simple lymph!

The frequent references in the literature to spontaneous chylous ascites following the ingestion of a heavy meal are also somewhat difficult to understand. Although experimental studies have shown that lymph flow in the thoracic duct is markedly increased after the ingestion of a fatty meal, the manometric pressure studies of Webb and Starzl[44] would suggest that rather dramatic elevations of intraductal lymphatic pressure can be produced without rupture of the intraabdominal or intrathoracic lymphatics. It would seem unlikely, then, that the increased flow associated with a heavy fat load in the intestine would be sufficient to rupture otherwise normal intraabdominal lymphatics.

There are several other facets of this clinical problem which have yet to be satisfactorily explained. The role of the lymphatic system in supplying the peripheral blood with lymphocytes and eosinophils is as yet poorly understood. Whether the depression of circulating lymphocytes which occurs with total obstruction of the lymphatic system has anything to do with the downhill course of the patient with chronic chylous ascites and/or chylothorax remains to be determined. Enzyme and absorption[16] studies of chyle with present advanced biochemical techniques, and the use of tagged radioactive substances, should add considerably to our knowledge concerning what is now a large area of abundant confusion.

SUMMARY

A case of chronic chylous ascites in childhood caused by a 2½-year-old appendiceal abscess is presented. Resection of the abscess wall and

excision of pelvic scar tissue resulted in a satisfactory clinical result. Several provocative paradoxes remain in considering the clinical syndrome of chylous ascites when the pathologic physiology of its production is examined in the light of our meager basic knowledge of the physiology of chyle.

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CARCINOMA OF URETER*†

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There have been reported from various clinics in recent years, several cases of ureteral tumors. Few cases were reported before 1932.[7, 8] Since 1955 more articles have appeared than during the

CASE REPORT

A 27-year-old white man was seen in the Urology Clinic because of right upper quadrant pain which had lasted 3 hours. Pain subsided and when seen

Fig. 1. Excretory urography demonstrating suspicion of lesion, right ureter

interval between 1932 and 1955. I do not think it can any longer be considered a rarity.[11]

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† This paper represents the personal viewpoint of the author and is not to be construed as a statement of official Air Force policy.

by a physician, he had a dull ache in the right loin. No other symptoms were present.

Because of right loin tenderness and the finding of red blood cells in his urine microscopically, an excretory urogram was taken. He was asymptomatic after the initial 3-hour attack.

Initial urogram (fig. 1) was suggestive of a filling defect in the right upper ureter. A retrograde

Fig. 2. Retrograde urography

urogram was then performed while the subject was an outpatient (figs. 2 and 3). Deformities are evident; in figure 2 the fingerlike projection of the filling defect may be seen.

The patient was admitted to the hospital on the 3rd day following the initial attack. Under spinal anesthesia a nylon loop catheter was passed into the right ureter. No material was recovered; therefore, a Johnson basket was passed and a piece of tissue 2 by 2 mm. was removed. No bleeding was noted but a no. 6 French ureteral catheter was left *in situ* for 24 hours.

The pathologic diagnosis was papillary transitional cell carcinoma, grade II.

The specimen consisted of blood and fibrin within which were enmeshed strips and fragments of epithelium as well as nests of epithelial cells. These cells, which generally show stratification, were uniformly rather large and cuboidal in appearance, with abundant cytoplasm, often show-

ing reticulation, fenestration, or vacuolization, either exclusively or in combinations.

The nuclei for the most part were large, regular and more or less centrally placed. Variations of nuclear size, staining intensity and chromatin content were readily seen, along with a rare mitotic figure. Several giant, multinucleate cells were observed.

The complete absence of stroma or subepithelial connective tissue did not allow for orientation of this material (figs. 4 and 5).

On the 6th day after the onset of symptoms, once it had been ascertained that all the blood chemistries, urine cultures and the chest survey were normal, a right nephro-ureterectomy was performed. Two incisions were made, a right loin incision and a midline suprapubic incision. A contiguous cuff of bladder to include the ureteral orifice was also excised and a cystostomy tube

Fig. 3. Retrograde urography, oblique view

employed. The latter was removed on the 5th postoperative day. Recovery was uneventful.

The specimen removed at surgery included kidney, ureter and cuff of bladder; grossly the kidney was normal. Multiple digitiform projections were noted within the lumen of the ureter, 4.5 cm. from the renal pelvis (fig. 6). The largest measured 1.7 by 0.3 cm. and the smallest, 0.9 by 0.2 cm.

Pathologic description. Sections through the mucosa of the renal pelvis revealed sclerosis and chronic inflammation of the subepithelial area; a granulating ulceration was noted at the ureteropelvic junction and in the proximal ureter.

The renal parenchyma was considered within normal limits.

The intact transitional epithelium was hyperplastic (more cellular than normal) with relatively uniform cells and nuclei, but with scattered minor variants throughout. Nests of identical epithelial cells were seen in the superficial and deeper connective tissue, but these were believed to be either artifacts of cutting or congenital nests. There was no suggestion of erosion.

Each of the grossly described polyps consisted of a central, vascular, dense connective tissue core covered on the periphery by stratified transitional epithelium, similar to that of the pelvic mucosa, but an increase of the minimally abnormal forms; some of the nuclei were unusually hyperchromatic; rare mitoses were seen. No invasion was recognized (fig. 7).

Cross sections of ureter at a slightly more distal level disclosed a lumen which contained cell nests and strips, admixed with blood, identical to the original biopsy material.

Fig. 4. Low power microscopic view of biopsy obtained by Johnson basket at cystoscopy (× 50).

The patient is only 9 months postoperative. He will be cystoscoped every 3 months for 2 years and every 4 months for another 3 years.

SUBJECT REVIEW

Incidence, age, sex and location. The reported cases do not exceed 500,[11, 13, 14] so we must assume that associated bladder tumors may be wrongly classified and the latter listed as a primary disease. Baker and Graf's[1] series confirm earlier reports[6] that tumor of the ureter is primarily a disease of the 5th and 6th decades; however, they reported 2 in the latter part of the 3rd decade. The case here presented was that of a man 27 years old. The youngest reported was aged 22 and the oldest, 81 years.[11] Male incidence is a predominant 4:1.[13] They occur 3 times more commonly in the lower third of the ureter,[5-7, 12]

but may be found in other segments. The upper third is less likely to be the site of disease. There is no predilection to right or left ureter. Three cases of bilateral ureteral carcinomas have been reported.[4] In the case presented, it arose in the upper third of the ureter, 4.5 cm. from the renal pelvis.

Diagnosis. Only 36 per cent are diagnosed preoperatively.[6, 10] Symptoms are varied and not specific. Hematuria, microscopic or gross, with or without colic, may be present.

The earliest finding is a deformity on the ureterogram. It may be picked up or suspected even on excretory urography, as was true in the case reported. Any goblet shaped defect in the ureteral course should make one suspect presence of the disease. The use of the Braasch bulb at the time of retrograde urography may help. Per-
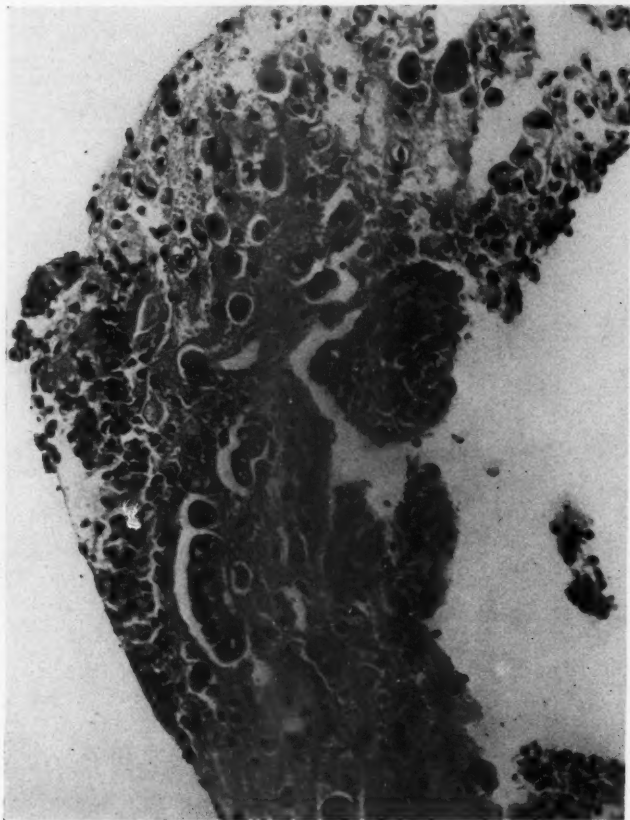
Fig. 5. Same section as shown in figure 4 ($\times$ 100).

sonally, I do not believe that the use of the Johnson basket as employed in this case should be a routine diagnostic procedure. The risks of complicating hemorrhage or rupture of ureter and dissemination of disease are too great.

Pathology. Classification of papillary or non-papillary may be made as to gross structure. Histologically, I concur with the classification of Whitlock and associates:[13] (1) papillary carcinoma, (2) papillary carcinoma and infiltrating, (3) non-papillary infiltrating carcinoma. Papillary growths in the urinary tract have the propensity to form recurrent growths and must be considered malignant.

O'Connor[9] took exception to Vest's[12] early article in which he related that benign tumors occur as epithelial growths showing no histologic evidence of malignancy. The former felt it not

justified to make a diagnosis of "benign" papillary tumors of the ureter. Others[3] believe that Vest's classification is a better guide. Earlier, however, Vest[12] recommented nephro-ureterectomy for this disease if malignancy was a question. Hamm and Lavalle[5] consider all tumors of the urinary tract malignant. Even with earlier classification in the 1940's, 3 times as many ureteral tumors were reported malignant as benign, when first examined microscopically.[6] In view of Scott's[11] extensive review of 182 cases with a high mortality rate, it seems that clinically we must consider all papillary tumors of the ureter malignant.

Treatment. Nephro-ureterectomy, with excision of a cuff of the contiguous bladder wall, is recommended by everyone. Before this decade a 2-stage operation was the method of choice since

FIG. 6. Gross specimen removed at surgery demonstrating tumor

operative mortality was 40 per cent in the 1-stage procedure.[10] In an unclassified group for this disease, it was 24 per cent in the 2-stage procedures.[11] The main causes of death from operation were listed as shock, pneumonia, paralytic ileus, myocardial failure and embolic phenomena. Reagan[10] reported a 5 per cent mortality with a 2-stage procedure. The first stage was a nephro-ureterectomy; the second, excision of bladder cuff or removal of distal non-involved ureter if that had been left behind at the first stage. Our 1-stage procedure consists of removing kidney, ureter and contiguous bladder cuff at one operation.

Follow-up periodic cystoscopy is a strict necessity. In view of the late recurrences, periodic cystoscopy should be performed over a 5-year postoperative period.

Results. No adequate follow-up of a large series of cases has been made. Those which have been adequately followed by various authors have provided the statistics mentioned earlier in this paper. Past results have been poor and discouraging. Recurrence of these tumors is as high as $33\frac{1}{3}$ per cent after removal of primary tumor, even by nephro-ureterectomy, sometimes occurring many years after surgery.[13, 14] In the early disease, *viz.*, papillary carcinoma without infiltration, the survival rate for 5 years following surgery is 66 per cent.[13] When the submucosa or muscularis layers are involved, the survival of 1 year is unusual in spite of surgery. Unfortunately, many tumors are advanced to this degree before symptoms are manifested.

Outlook for future. We are optimistic although past results have been poor. One gathers from
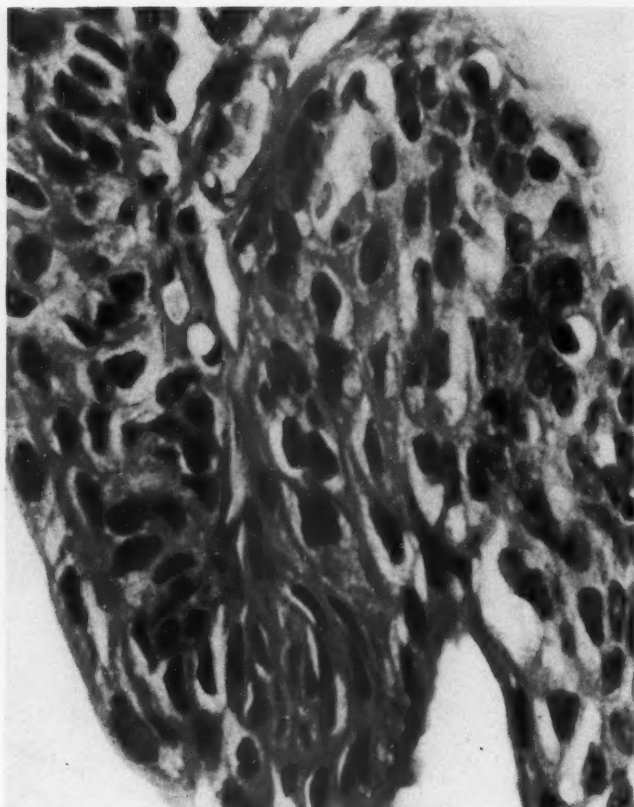
Fig. 7. High power magnification of specimen removed at surgery (× 430).

TABLE 1

Incidence of reporting of cases of carcinoma of the ureter

Total No. of Cases	Year by which Reported	Additional No. of Cases Reported	No. of Years in Period Elapsed
8	1902		
33	1922	25	20
36	1924	3	2
49	1930	13	6
61	1934	12	4
133	1936	72	2
139	1939	6	3
182	1943[11]	43	4
312	1955[13]	130	12
454	1958[14]	142	3

reviewing the literature of 50 years of treatment of this disease that earlier and more radical treatment is being given at this time. Supportive anesthesia and revised postoperative treatment as well as the use of antibiotics have decreased the immediate postoperative mortality.[2, 14]

Then, wherein does our problem lie? Diagnosis has not been made early enough in the past. It appears that, as a result of reports such as this, more cases are diagnosed and reported. Cases are being reported at a greater frequency. A summary of reported cases reveals this (table 1).

The increase in the number of cases reported has been attributed to advances in diagnostic techniques and more frequent autopsies.

The growth of the specialty of urology with its concurrent teaching programs, the increased dis-

semination of information through medical literature, and the encouragement of our residents to report interesting cases have offered and continue to offer hope for early diagnosis and radical treatment, and an improved mortality rate.

SUMMARY

A case of early carcinoma of the ureter is presented. A diagnosis of an intraureteral mass was suspected by excretory urograms, and proved by retrograde pyelography, but was diagnosed from a biopsy obtained by using the Johnson basket. Use of the Johnson basket, however, should not be considered a routine means of obtaining such tissues.

General statistics for a 50-year period as well as recommendations for diagnosis and treatment of this disease are presented. The disease is not as rare as formerly believed. Early diagnosis and radical surgery are recommended for cure.

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PERFORATED DUODENAL ULCER DURING STEROID THERAPY: REPORT OF FOUR CASES, INCLUDING TWO GIANT PERFORATIONS*

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Cortisone and its synthetic analogues, prednisone and prednisolone, have brought marked improvement in many diseases, but there have been some undesirable side effects. Peptic ulceration of the stomach and duodenum appear frequently as complications of the use of these drugs. Perforated duodenal ulcers in patients on steroid therapy rarely have been reported in the literature. The incidence may be higher than one would conclude. According to reports, gastric ulcer appears to be more common than duodenal ulcer.

There seems to be more than a casual relationship between the development of peptic ulcer and steroid therapy. Some investigators feel that prednisone and prednisolone have an especially potent ulcerogenic affect.

Recently we have had experience with 4 cases, each receiving steroids for a different disease. The 1st and 4th cases are most unusual because of the finding of giant ulcers with perforations.

CASE REPORTS

Case 1. A 39-year-old white woman was admitted to the City of Memphis Hospitals on February 11, 1958. She had been treated for rheumatoid arthritis for 20 years and during the past few months had received 10 mg. of prednisolone, daily. Several months before admission she began to have tarry stools. Gastrointestinal series revealed a duodenal ulcer and ulcer therapy was instituted. On February 13, 1958, she began to have severe epigastric pain. The patient's abdomen became rigid and vomiting occurred. On admission to the hospital the lateral decubitus film of the abdomen revealed free air in the peritoneal cavity (fig. 1). A tentative diagnosis of perforated duodenal ulcer was made, and laparotomy was performed. There was found a giant duodenal ulcer which had perforated into the peritoneal cavity (fig. 2). This perforation was 3.5 cm. in diameter and it involved the lateral and anterior wall of the first portion of the duodenum. There was a minimum amount of reactive tissue in the area of the perforation. The abdominal cavity contained approximately 500 cc.

* From the City of Memphis Hospitals and the University of Tennessee College of Medicine.

of gastric contents with minimum reaction in the peritoneal cavity. In view of the size of the ulcer and the fact that the patient would have to be maintained on cortisone indefinitely, it was felt that gastric resection should be performed. A two-thirds subtotal gastrectomy was performed with an anterior Hofmeister anastomosis. The patient tolerated the procedure well and had an uneventful postoperative course. She was maintained on steroids during the postoperative course and after her discharge from the hospital. Follow-up in the outpatient department revealed that the patient is getting along well and is free of ulcer symptoms.

Case 2. An 11-year-old colored girl was admitted to the City of Memphis Hospitals on October 1, 1958, complaining of stiff joints which had been present for 6 weeks before admission. Positive findings on physical examination revealed a chronically ill, emaciated child with moderate limitation of motion of the shoulder and hip joints, pretibial edema of the right leg and a tender right ankle. There were areas of hyperpigmentation on both malar areas. An apical systolic murmur was present. On October 13, 1958, muscle biopsies were taken from the right arm and left leg from which a diagnosis of dermatomyositis was made.

The patient was placed on prednisolone steroids, 15 mg. q.i.d. and later reduced to 10 mg. q.i.d., with an excellent response. However, on November 25, 1958, she complained of abdominal pain and a diagnosis of perforated peptic ulcer was made. At laparotomy the patient was found to have a 3-mm. perforation in the anterior wall of the first portion of the duodenum. This was closed by the Roscoe-Graham technique. The patient had an uneventful postoperative course, but was gradually weaned from her steroid therapy during the next month, and was discharged from the hospital in good condition on December 20, 1958.

Case 3. A 41-year-old colored woman was admitted to the City of Memphis Hospitals on July 22, 1958, with bilateral pleural effusions due to metastatic carcinoma of the breast. The patient had been on prednisone, 10 mg. daily, for 2 months, as well as on testosterone. Radical mastectomy had been performed September 12, 1956, and oophorectomy on February 5, 1957.

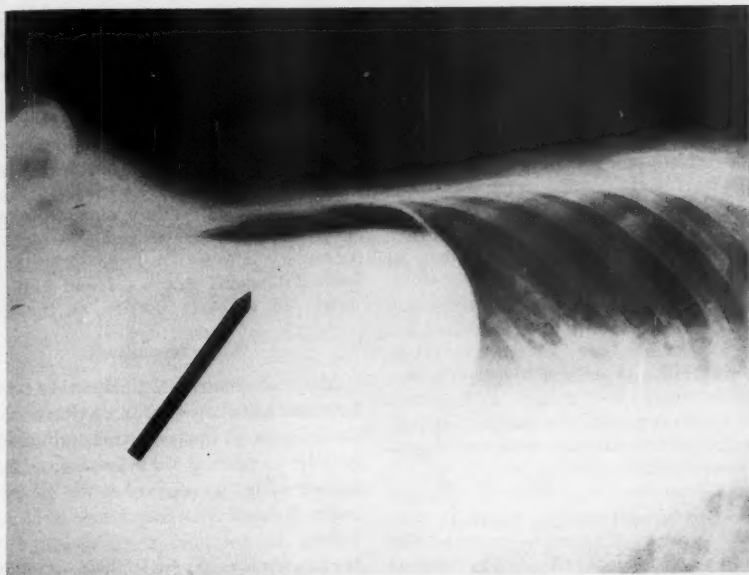The patient's treatment in the hospital consisted of multiple thoracenteses and instillation

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FIG. 1. Air fluid level is demonstrated on left lateral decubitus film. Free air in peritoneal cavity may be more important diagnostic point when symptoms are masked.
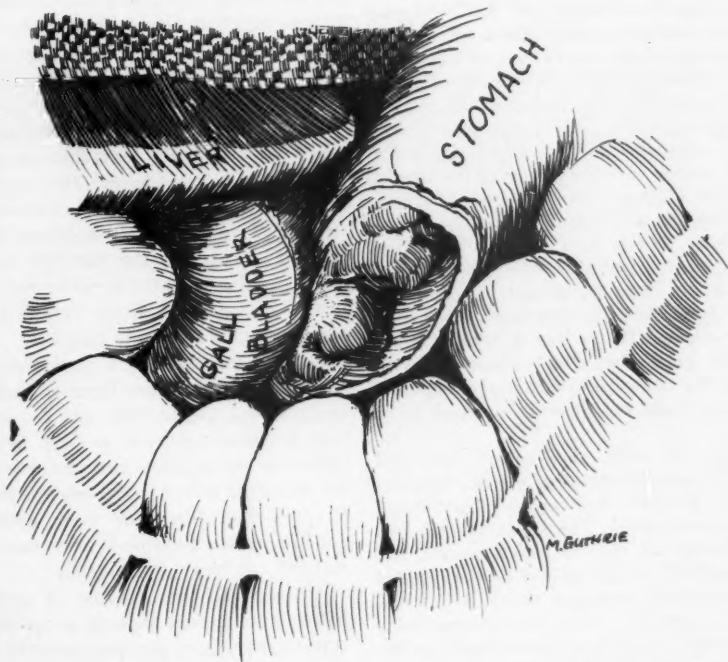
FIG. 2. Ulcer has completely eroded entire anterior and most of the lateral walls of duodenum. Inflammatory reaction in area is minimal.

of triethylenethiophosphoramide into the pleural cavity. The patient's general condition improved with thoracenteses but the fluid again rapidly accumulated. On August 26, 1958, the patient vomited a small amount of blood and complained that her appetite was very poor. Abdominal findings consisted chiefly of a very large liver, palpable down to the level of the umbilicus, but no tenderness was present. The patient's course was downhill in spite of her being placed on an ulcer regime and being given blood transfusions. She died on September 2, 1958.

Autopsy findings revealed metastatic adenocarcinoma to the chest wall, right upper extremity, liver, left breast, left lung, left thoracic cage, pituitary, right adrenal and aortic lymph nodes. A 1-cm.-wide ulcer was found in the first portion of duodenum, with the gall bladder adherent to the perforation. No evidence of generalized peritonitis was present.

Case 4. A 6-year-old colored male was admitted to the City of Memphis Hospitals on April 21, 1958, with edema of 4 days' duration. In February 1958 the patient had an influenza-like disease followed by hematuria and swelling. He was treated by his family physician, with some improvement.

On admission there was periorbital and pitting edema of the pretibial areas. Urinalysis showed 4+ protein, numerous casts, 2 to 6 RBC, and 4 to 6 WBC, per high power field. Total serum protein was 3.3 gm. with an A/G ratio of 1.0 to 2.3. The serum cholesterol was 622 mg. A diagnosis of nephrotic syndrome was made and the patient was placed on prednisolone, 5 mg. q.i.d. There was noted some intermittent improvement for the next 2 months with the dosage of the steroid being doubled. However, the edema soon returned, along with ascites. A change from prednisolone to hydrocortisone, 50 mg. q.i.d., was made and the patient became hypertensive. The patient's condition gradually deteriorated and anasarca was noted on July 24, 1958. The hydrocortisone dosage was increased, and the patient developed hypocalcemia and hyperkalemia. This was treated with glucose, insulin and calcium with a good response. The hydrocortisone dosage was decreased to 50 mg. t.i.d. On August 10, 1958, the patient developed hematemesis and abdominal pain with radiation to the right shoulder. A diagnosis of perforated peptic ulcer was made. The serum protein was 2.2 gm. Because of the low serum protein and critical condition of the patient it was decided that nonoperative treatment should be carried out. With nasogastric suction, intravenous fluids and antibiotics, there was improvement in the abdominal symptoms. On August 26, 1958, a switch was made to methylprednisolone, 20 mg. daily,

which was gradually decreased to 12 mg. daily. There was a gradual increase in the ascites and the proteinuria, and the patient became uremic. The condition gradually deteriorated, and the patient died on September 21, 1958.

Autopsy findings revealed cryptococcal meningitis and uremia which the pathologist believed to be the cause of death. The patient was found to have an atypical picture of acute glomerulonephritis, marked ascites and a 3- by 4-cm. right subhepatic abscess. A large (2 by 3 cm.) perforated duodenal ulcer was found on the posterior aspect of the first portion of the duodenum.

DISCUSSION

Many clinicians feel that patients who are to be placed upon any type of corticosteroid therapy should have an upper gastrointestinal series done in order to rule out a duodenal ulcer. If there is a history of peptic ulcer or if the gastrointestinal series demonstrates ulceration, it is usually advisable to withhold these drugs. Patients on corticosteroids may react best on an ulcer diet and, in many cases, ulcer medication, as a routine measure.

If more care is taken in selection of the patient and the dosage of the drug some ulcerations may be avoided. With the onset of the mildest symptoms suggestive of ulcer, the dosage of the medication should be decreased and the drug stopped if at all possible. Once perforation has occurred it may be necessary during and immediately after surgery to give larger doses than the patient had been taking before surgery. The selection of the operation to be performed will depend on whether or not the patient is to continue steroids indefinitely. This was the situation in case 1 in which gastric resection was performed. If the drug can be discontinued simple closure may be the treatment of choice, as in case 2.

Surgical treatment of a giant ulcer may be a more difficult problem because these are not easily closed. Again, this was the situation in case 1. Development of a giant ulcer may be related to the minimal inflammatory reaction in the duodenal wall. Surgical intervention is urged in perforated ulcers in these patients when possible, since a giant perforation may be present and will not "seal" itself readily.

Although the exact cause of ulcerations in patients on steroid therapy is unknown, some investigators have discussed several aspects of their formation. Acid pepsin secretion is usually increased, as well as susceptibility of the con-

nective tissue to acid pepsin digestion. There seems to be a decrease of viscosity, as well as quantity, of the gastric mucus, with resulting breakdown of the so-called "mucous barrier." Some vascular influence may occur, resulting in focal ischemia, before the development of an ulcer.

Another antiarthritic compound, phenylbutazone, appears more often in the literature as being associated with perforated peptic ulcer. The salicylates, also, have been incriminated as a cause of ulceration of the stomach and duodenum.

SUMMARY

1. Four cases of perforated duodenal ulcer in patients on corticosteroid therapy are reported, including two patients with giant duodenal ulcers and secondary perforations.

2. Symptoms of an ulcer in steroid treated patients may be absent or diminished before and after perforation.

3. A minimum of local reaction in the area of the duodenum is thought to coincide with the findings of previous investigators.

4. When possible, early surgical intervention is urged since a giant perforation may be present which will not "seal" itself on nonoperative treatment.

5. Subtotal gastric resection or simple closure was performed. Good healing was obtained in the surgically treated patients in spite of large doses of steroids.

6. Primary gastric resection should be considered in patients on long term steroid therapy undergoing surgery for perforated duodenal ulcers. It is believed to be the procedure of choice in a giant perforation which cannot be closed readily.

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ACCIDENTAL SWALLOWING OF A PARTIAL DENTURE AND ITS SPONTANEOUS PASSAGE THROUGH THE GASTROINTESTINAL TRACT*

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Numerous types of foreign bodies have accidentally or purposely been swallowed and have been eliminated spontaneously through the gastrointestinal tract. The following case is presented to emphasize that even an irregularly shaped body with projecting, sharp points may be treated expectantly.
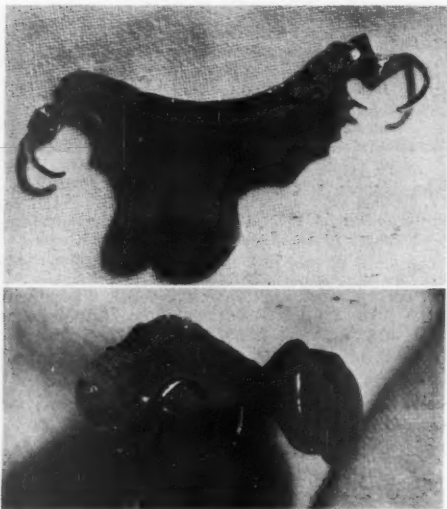

FIG. 1. Photographs of the accidentally swallowed partial denture which consists of two teeth, a metallic support, and a sharp clasp at each end. Note the projecting, sharp points on the clasps.

CASE REPORT

History. During the evening of October 10, 1958, a 26-year-old white woman inmate of the Columbus State School sneezed and swallowed a partial denture (fig. 1). After this accident, the patient did not have pain, nausea, or vomiting. On the

morning of October 13, 1958, 2½ days later, surgical consultation was requested.

Past history. In 1952, a partial denture for the superior anterior teeth had been prepared and, since that time, had been worn without difficulty. The location of the denture in position may be seen in figure 2, a roentgenogram taken in 1955.

Since infancy, the patient had been a hydrocephalic.

Physical examination. The patient was well nourished and appeared to be in relatively good health. The abdomen was not distended; no masses or soft organs were palpable; there was no tenderness; and bowel sounds were normal. Vaginal and rectal examinations were within normal limits. In so far as the present illness is concerned, the remainder of the physical examination was not remarkable.

Laboratory data. At the time of admission, the hemoglobin was 12.4 gm. per 100 ml.; the total leukocyte count was 11,150 with 68 per cent segmented neutrophils, 2 per cent nonsegmented neutrophils, 29 per cent lymphocytes and 1 per cent eosinophils. Admission urinalysis indicated a specific gravity of 1.020, a reaction of 6.0, a clear, yellow appearance, no albumin, no sugar, no acetone and 2 to 3 leukocytes per high power field.

Hospital course. At the time of initial surgical consultation on October 13, roentgenograms indicated that the denture was in the left upper abdominal quadrant.

The patient was admitted to the Columbus State School Hospital for observation. A Levin tube was inserted into the stomach, and was attached to suction. No visible blood was aspirated through the Levin tube. During the next several days the Levin tube was removed and the position of the denture was followed with daily roentgenograms (figs. 3 and 4). The patient was allowed to eat and she was given a variety of enemas. She did not show any signs of intestinal obstruction, bowel perforation, or peritonitis and, on the morning of October 16, the denture was passed spontaneously in a mass of feces which did not grossly contain any blood.

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Fig. 2. Skull roentgenogram which had been taken on April 1, 1955, for study of the hydrocephalus. The partial denture is indicated by the arrows.

Fig. 3. Roentgenograms demonstrating position of the partial denture which was swallowed on October 10, 1958. (*Top*) Roentgenogram, taken on the evening of October 13, shows the denture in the left upper abdominal quadrant and a Levin tube in the stomach. (*Bottom*) October 14, indicates that the denture is still in the left upper abdominal quadrant but that it has rotated on its longitudinal axis.

The patient has not had any permanent adverse effects from the swallowing of this foreign body.

COMMENT

Operative intervention was considered primarily because of the projecting sharp points of

Fig. 4. October 15, a lateral abdominal roentgenogram presents the denture low in the abdominal cavity; on October 16, the denture was found in a mass of feces.

the denture and not because of the size of the object. Fear was entertained that these sharp points might penetrate the gastrointestinal tract at the pyloric or ileocecal valves or at the duodenal or duodenojejunal curvatures. With conservative management, however, the partial denture slowly moved through the gastrointestinal tract and, 6 days after being swallowed, it was found enclosed in a mass of feces.

SUMMARY

An irregularly shaped object with projecting points may be accidently swallowed and, without operative intervention, may pass through the gastrointestinal tract.

In the case reported, a partial denture was swallowed during sneezing and, at defecation 6 days later, was found in the feces.

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LYMPHOSARCOMA OF THE BREAST: DISCUSSION AND PRESENTATION OF A CASE

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Sarcomas of the breast are of two main varieties, the most common arising from a pre-existing pericanalicular or intracanalicular adenofibroma, and the other arising from the interlobular fibrous tissue. Sarcomas arising from other components of breast tissue such as liposarcoma, lymphosarcoma, myosarcoma and angiosarcoma are rarely encountered. A lymphosarcoma which makes its appearance as a mass in the mammary gland may be the first sign of a systemic neoplastic process. It is necessary, therefore, that such cases be differentiated from those of adenocarcinoma in order that appropriate treatment may be instituted. Other such systemic neoplasms which may first appear as a mass in the breast or axillary region include chloroma, with and without accompanying blood changes, lymphatic leukemia and lymphogranuloma of the Hodgkin type. Rarely, a lymphogranuloma or lymphosarcoma has appeared as a localized mass in the mammary gland without evidence of coexisting systemic disease and the patient has failed to show evidence of a more extended neoplastic process on long term follow-up studies. Somewhat more unusual was the patient of Judson,[7] a 62-year-old woman who was found to have simultaneous adenocarcinoma and lymphosarcoma in one breast.

Although the total number of cases of sarcoma of the breast is still small, the pathologic variety is great. Approximately one-half originate in the fibrous stroma of the gland, with the other forms arising from fat, vascular structures, other mesenchymal derivatives or the nerve sheaths. There are also mixed tumors.

Fox[2] found some 510 mammary sarcomas reported in the literature, and he estimated their frequency as 1.6 per cent of mammary tumors. Wellbrock[9] reported only 29 sarcomas in a series of 7763 mammary lesions at the Mayo Clinic. Sailer[8] estimated the proportion as 1 sarcoma to 100 mammary carcinomas. From these studies it can be determined, therefore, that lymphosarcoma of the mammary gland, and especially

that lesion which is not part of a generalized disease process, is rare indeed.

In comparison with the long duration of symptoms often noted in fibrosarcoma, symptoms in lymphosarcoma of the breast are brief. These tumors, according to Geschickter,[3] grow rapidly, are soft or doughy in consistency and for a time remain freely movable. Rapid enlargement or multiple nodules in one or both breasts soon follow. The axillary, inguinal or mediastinal lymph nodes may become enlarged, and ascites and edema may occur in the lower extremities with extension of the disease to the mediastinal and abdominal lymph nodes.

On section, lymphosarcomas are seen to be homogenous, cellular growths. Microscopic studies show little or no stroma. The tumors are composed of tightly packed lymphoid cells of varying sizes with numerous mitotic figures.

CASE PRESENTATION

A 55-year-old white woman first noticed a painless mass in her right breast 5 weeks before admission. She stated that she had lost 65 pounds while under the supervision of her doctor. The sudden appearance of a mass was the first indication of any specific lesion being present. The system review and history were essentially negative and the family history was noncontributory. The patient was a well developed, moderately obese woman who appeared quite healthy. Her blood pressure was 140/90 and the pulse was 82 and regular. Her heart and lungs were normal. On inspection of the breasts it was noted that the left was more pendulous than the right. On palpation there were two large, firm, irregular masses present in the upper outer quadrant of the right breast which were movable and had no apparent attachment to the skin. No regional adenopathy or skin changes were noted. The left breast and axilla were normal. No cervical or supraclavicular adenopathy was noted. The peripheral blood showed a hematocrit of 42 per cent. The leukocytes numbered 8950, with 61 per cent segmented forms, 36 per cent lymphocytes, 2 per cent monocytes and 1 per cent basophils. The urine was normal.
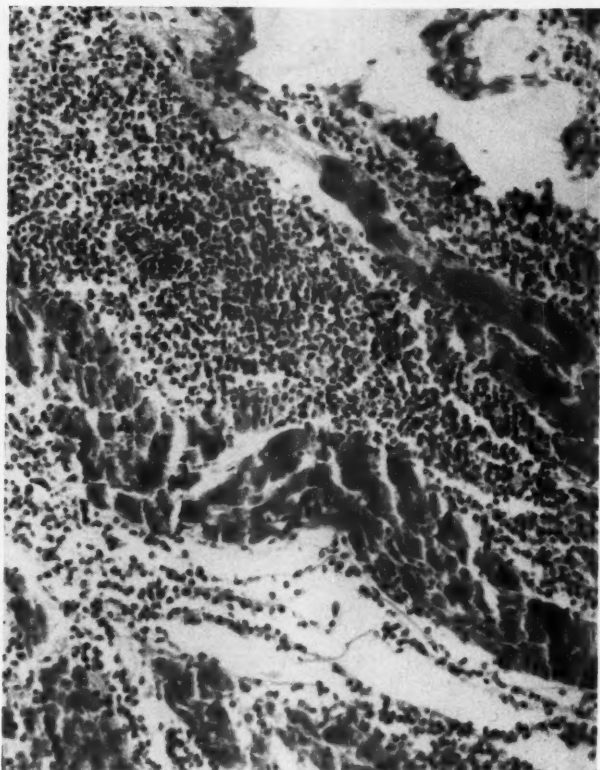
FIG. 1. Section showing infiltration of cardiac muscle by metastatic lymphosarcoma, the primary lesion being in the breast.

A chest film showed some calcification in the arch of the aorta, but otherwise no abnormalities were noted. There was no evidence of metastatic disease.

On the 2nd hospital day surgery was performed and elliptical incisions were made around the right breast. Skin flaps were reflected and the breast entirely removed. It was noted that there was one large lymph node in the axilla. This was sent to the laboratory and the pathologist reported that, on frozen section, the lesion appeared to be lymphosarcoma. The pathologist felt that two more masses demonstrated in the breast were the same type lesion. He deferred the final decision until after the permanent sections were made. The wound was then closed with retention sutures and silk. The patient made an uneventful recovery. Paraffin sections of the breast tumors showed groups of closely packed reticuloendothelial cells with large vesicular nuclei and prominent nucleoli. There was a fair amount of basophilic cytoplasm and these cells showed loss of polarity. Many of the nuclei presented mitotic figures. These groups of cells were surrounded by a dense, fibrous connective tissue stroma showing lymphocytic and plasma cell infiltration. The section of the lymph node taken from the axilla showed an intact, thin, fibrous connective tissue capsule. The lymphoid stroma showed several lymph follicles with active germinal centers. One section showed obliteration of the follicular pattern, and lymphocytes and reticuloendothelial cells were diffusely arranged in this area. The impression was of sarcoma of the reticulum cell type involving the right mammary gland with metastases to regional axillary lymph node.

On the 7th postoperative day the patient was again taken to the operating room, where a radical procedure was done. It had been decided that the prognosis could be improved if as much of the neoplastic tissue as possible were removed. Both pectoral muscles were excised and an axillary dissection carried out. The recovery was again uneventful. Sections made from specimens re-

moved at this secondary procedure revealed no malignant change. The patient was discharged as recovered on the 10th day after the secondary procedure. At no time during this patient's hospital stay did her clinical studies indicate that the lymphosarcoma involving the right breast was anything other than a lesion confined to that structure.

In view of the malignant nature of this lesion it was decided to give the patient the additional benefit of x-ray therapy. This was begun 1 month after the second operation and was given for a period of 8 days over two areas of the right breast region. It was during this treatment that splenomegaly was noted, for which she was given an additional 9 days of x-ray treatment over the area of the spleen. Following the 9th day of treatment the spleen was barely palpable.

Immediately following her radiotherapy the patient did quite well and, in fact, gained 20 to 30 pounds. Within 7 months, however, she was again in the hospital with a progressive pleuritic type pain in the left chest, which in a short time became rather extreme in character. She also complained of some numbness in the left arm and hand. After treatment with x-rays and nitrogen mustard she improved considerably. She was admitted 2 months later for x-ray treatment to the liver and spleen. There was right pleural effusion at this time and auricular fibrillation. The depression of her leukocytes was felt to be secondary to therapy. She entered the hospital for the last time, 11 months following her first admission, with a right pleural effusion with increased shortness of breath. Bone marrow studies at this time revealed anemia, but no definite malignant cells were demonstrated. She became progressively worse and about 3 weeks following her final admission she died from extensive terminal involvement of all organs. The slides from the original breast lesion were reviewed and the tumor cells were found to be identical with the tumor cells that infiltrated all the organs noted at the time of

autopsy. The findings in this case were felt to be compatible with a primary lymphosarcoma of the breast with extensive generalized spread.

SUMMARY

A general discussion of the subject of lymphosarcoma of the breast is presented along with a review of the literature. The case history of a 55-year-old white female patient with an isolated lymphosarcoma of the right mammary gland, which was not found to be part of a generalized disease process, is presented . This patient underwent repeated therapy with x-ray and nitrogen mustard over a period of approximately one year until she died from extensive terminal involvement of all organs.

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A CRITICAL EVALUATION OF DIRECT SURGICAL PROCEDURES IN THE TREATMENT OF OCCLUSIVE PERIPHERAL VASCULAR DISEASE*

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Restorative operations for the treatment of atherosclerotic occlusion of peripheral arteries have been in use for more than a decade, but there still remains lack of agreement regarding the relative merits of the various procedures, indications for their use, and the long term results of treatment.[2, 3] It is not certain that these questions can ever be answered satisfactorily because of the many variables involved. Notable among these is the natural history of the disease itself,[4] characterized by sporadic progression and the production of symptoms largely through thrombotic complications. Regarding the results of treatment, it is extremely difficult to separate failures of the operative procedure itself from those which follow progression of the disease. Nevertheless, in efforts to evaluate our experience with these procedures, all cases have been reviewed in which bypass grafts or thrombointimectomy have been employed during the past $2\frac{1}{2}$ years. This report is concerned with an analysis of these cases.

METHODS AND MATERIAL

As indicated above, two types of procedures were employed; namely, bypass grafting and thromboendarterectomy, or more properly, thrombointimectomy. Crimped nylon grafts were used almost exclusively for bypass operations. Technique of bypass, previously described,[1] consists of an end-to-side anastomosis of the graft to the involved artery above and below the obstruction. In the case of aorto-iliac occlusion this procedure consisted in laying the graft on the aortic bifurcation with anastomosis to the front of the aorta above and to the iliac, femoral or popliteal arteries below. In some instances, in which there

was considerable inflammatory reaction about the aortic bifurcation, the aorta above the obstruction was divided, the distal end closed, and an end-to-end anastomosis performed between the aorta and the graft. Thrombointimectomy was performed through multiple longitudinal arteriotomies when there was aorto-iliac occlusion and by the use of intraluminal wire strippers for femoral-popliteal occlusion. Anticoagulants were not utilized during or after bypass operations but were employed during thrombointimectomy.

The presence and extent of the occlusive process were usually determined by arteriography except in some cases of complete aortic occlusion and in femoral-popliteal occlusion when the limb was in jeopardy. In some instances, examination of the popliteal bifurcation was made initially even though an arteriogram suggested extension of the occlusive process beyond this point (table 1).

AORTO-ILIAC OCCLUSION

Since July 1956, 24 patients with aorto-iliac disease have been treated (table 2). In 14 instances a bypass graft was used, extending from the aorta proximally to the femoral or popliteal artery below. Of these procedures, 12 were immediately successful in that there was restoration of blood flow with palpable pulses in the lower extremities. Of the 12 functioning grafts, 1 subsequently became infected and was removed and in 2 patients the graft became occluded. In these 2 the grafts extended from the aortic bifurcation to the popliteal artery, and both ceased to function about 6 months after implantation. The remaining 9 patients have had significant improvement in their symptoms and restoration of blood flow to the lower extremities has been maintained for periods varying from 6 months to 2 years. There were two deaths in this group. One occurred shortly after operation, consisting of an aorto-femoral bypass graft of the "onlay" type. The second death occurred several months after operation and resulted from infection of an ilio-femoral bypass.

TABLE 1

Occlusive disease

	Number of Cases	Graft	Thrombo-intimec-tomy
Aorto-iliac............	24	14	10
Femoral-popliteal.....	41	26	15*
Total..............	65	40	25

* Three were in patients with thrombosed grafts.

TABLE 2

Results: aorto-iliac occlusion

	Graft	Thromboin-timectomy
Successes		
Early......................	12	10
Late......................	9	10
Failures		
Early......................	2	0
Late......................	3	0

Thrombointimectomy was performed in 10 patients with aorto-iliac occlusion. All of these operations restored blood flow and there have been no late failures in this group. Among the 10 cases, thrombointimectomy was performed on the abdominal aorta and iliac arteries in 5, and in 5 this procedure was extended to the popliteal arteries.

FEMORAL-POPLITEAL OCCLUSION

In this series there were 41 cases of occlusion involving the femoral and popliteal arteries (table 3). In contrast to the patients with aorto-iliac occlusion in whom operation was undertaken primarily for symptomatic relief, an attempt to restore blood flow was often made in this group because of impending or established necrosis of tissues. In 26 cases a bypass graft was utilized. Among these, 20 were immediately successful in that blood flow was restored as indicated by palpable pedal pulses, relief of symptoms and healing of necrotic areas. There was, however, a high rate of subsequent occlusion in this group (table 4). Thus, in 15 cases the grafts are known to have become occluded at periods ranging from 6 months to 2 years; 2 patients could not be

TABLE 3

Results: femoral-popliteal occlusion

	Graft	Thromboin-timectomy
Successes		
Early......................	20	11
Late......................	3	11
Failures		
Early......................	6	4
Late......................	15	0

TABLE 4

Femoral-popliteal grafts, follow-up

No follow-up.................................	2
Failures	
< 6 months...............................	6
6–12 months..............................	3
1–2 years.................................	6
Successes	
9–18 months..............................	3

followed and in 3 the grafts are still functioning for periods from 9 to 18 months.

Thrombointimectomy of the femoral and popliteal arteries has been performed in 15 cases; 11 of these operations were immediately successful whereas 4 were unsuccessful. Of these, 2 of the failures occurred in patients who were reoperated upon following late failure of a bypass graft. In these 2, thrombointimectomy was attempted but was unsuccessful. Of the 11 patients in whom thrombointimectomy was initially successful, no subsequent occlusion has occurred during periods of observation ranging from 2 to 18 months.

DISCUSSION

As emphasized previously, the majority of cases of aorto-iliac occlusion fall into one of two groups.[2] Those cases in which occlusion is complete generally have patent arteries distal to the occlusion and relief of obstruction usually is followed by excellent results. The fact that a majority of these patients are in the middle decades of life and in their wage earning years, constitutes an indication for operation in most instances. Few of these people have symptoms of coronary or cerebral atherosclerosis so that the hazard of operation is not great and the prognosis in terms of definite relief of symptoms is extremely good. On the other hand, in the group with partial aorto-iliac

occlusion, atherosclerosis is almost always extensive, and simultaneous involvement of coronary and cerebral vessels is frequently present. Furthermore, this form of the disease is encountered most often in the later decades of life, usually near or beyond the end of the wage earning period. The risk of operation is considerably greater in this group and the operation itself is often more difficult, with results more uncertain, than in the patients with complete occlusion. It is in this group of cases of partial occlusion that confusion arises regarding the indications for operation since rarely does the opportunity for relief of symptoms alone justify the increased risk of operation to these elderly patients.

This small series of cases of aorto-iliac occlusion demonstrates that either bypass or thrombintimectomy may be successfully employed to restore blood flow to the lower extremities. Recent experience suggests that there is a somewhat greater incidence of late failures following the use of grafts than with thrombointimectomy. Furthermore, infection of synthetic grafts, although infrequent, constitutes a serious hazard to the patient.

Although thrombointimectomy is preferable, certain technical considerations may influence the decision in favor of a bypass graft. Thrombointimectomy is usually a more time consuming procedure; where the patient's general condition requires that the duration of operation be reduced, a bypass graft should be utilized. Finally, the condition of the diseased blood vessels may preclude thrombointimectomy. Thus, where there is extensive medial calcification, removal of the occluding atheromatous and thrombotic material
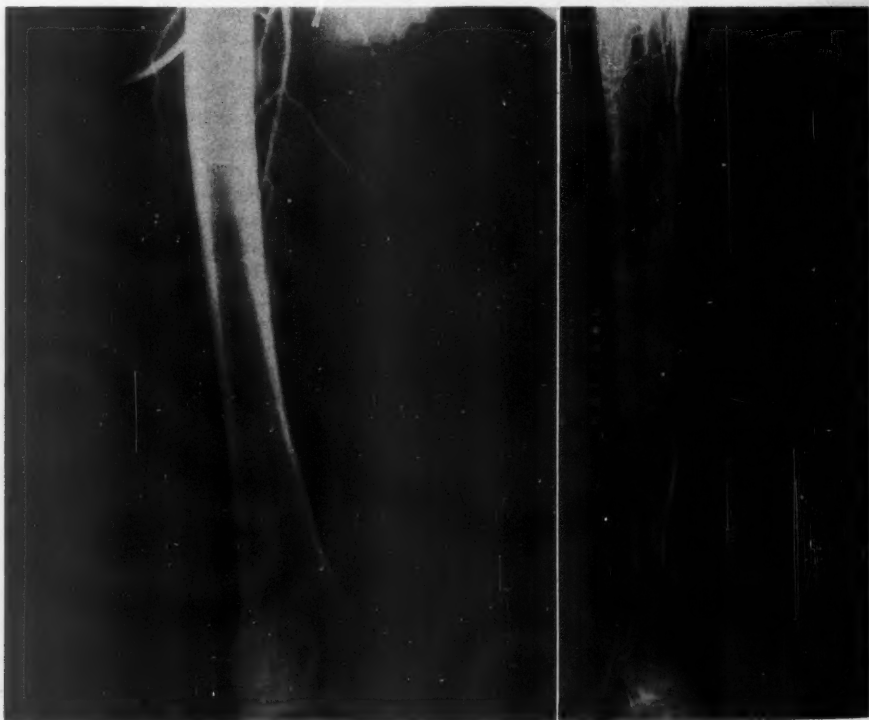
FIG. 1. After occlusion of a femoral bypass graft had occurred, a femoral arteriogram (*left*) demonstrates complete lack of filling of the superficial femoral artery and the popliteal artery. At exploration of the popliteal artery, however, a direct popliteal arteriogram (*right*) shows the popliteal artery patent and communicating with an extensive arterial bed in the leg.
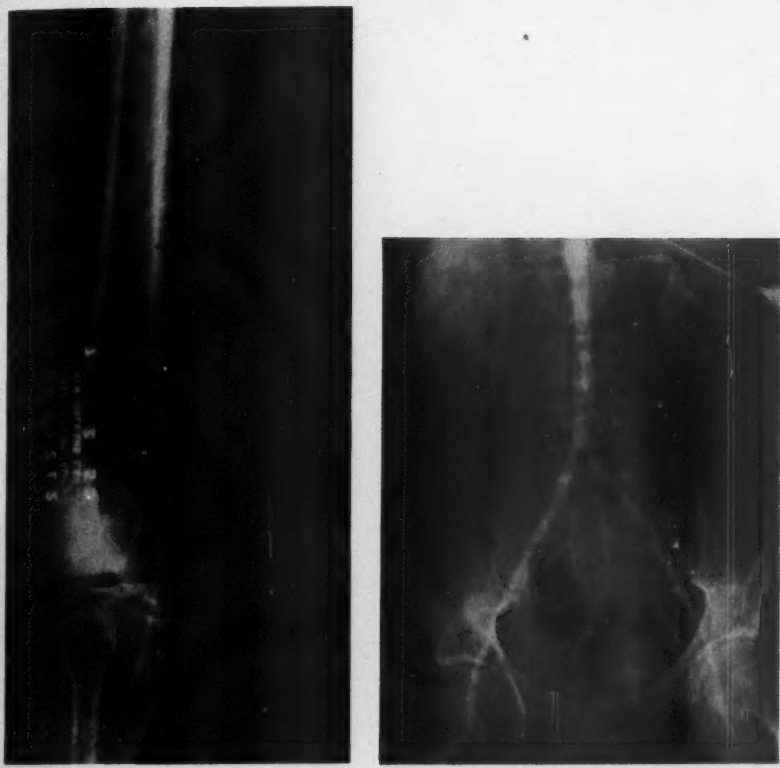
FIG. 2. A 65-year-old man with claudication, rest pain, and cutaneous gangrene had femoral artery occlusion with good popliteal "run off" area demonstrated on femoral arteriogram (*left*). Because of some diminution of common femoral pulse on that side, an aortogram (*right*) was made which shows partial occlusion in the left common iliac and at the iliac bifurcation. Thrombointimectomy from aorta to the popliteal restored pedal pulses. Failure to recognize a compromised source of "run in" may result in early failure from inadequate flow and pressure or late failure from thrombosis at the sites of partial occlusion.

together with the calcium deposits leaves an arterial wall composed only of adventitia. In cases where an aneurysmal dilation is superimposed upon occlusive lesions, thrombointimectomy leaves little mural substance for repair. Therefore, in the presence of extensive calcification or aneurysmal dilation, a bypass procedure should be used.

Because of the low operative mortality and morbidity and the gratifying results, the indications for operation are broad when the occlusive process is complete and confined to the aorto-iliac area. Extension of the disease beyond the external iliac artery, however, requires more careful evaluation since results in these cases are less satisfactory. In general, if symptoms are severe in

active, gainfully employed patients, operation should be undertaken even in the presence of an extensive occlusive process. If involvement is unilateral, thrombointimectomy of the common iliac, external iliac, internal iliac, and femoral arteries is advisable. When the occlusive process is bilateral, restoration of blood flow into both common and profunda femoral arteries is accomplished initially and subsequently femoral thrombointimectomy may be done.

Whereas the result of direct operations for aorto-iliac occlusive disease is generally good irrespective of the type of procedure employed, there was a striking difference in the results obtained with these two methods in femoral-popliteal occlusion. In view of our experience and that of

others, thrombointimectomy apparently is the procedure of choice in the treatment of occlusion of arteries of medium or small size.

In our cases, the causes of failure of bypass graft were varied. In most instances, occlusion of the graft developed at the proximal or distal anastomosis and rarely was occlusion due to progression of atherosclerosis in the popliteal
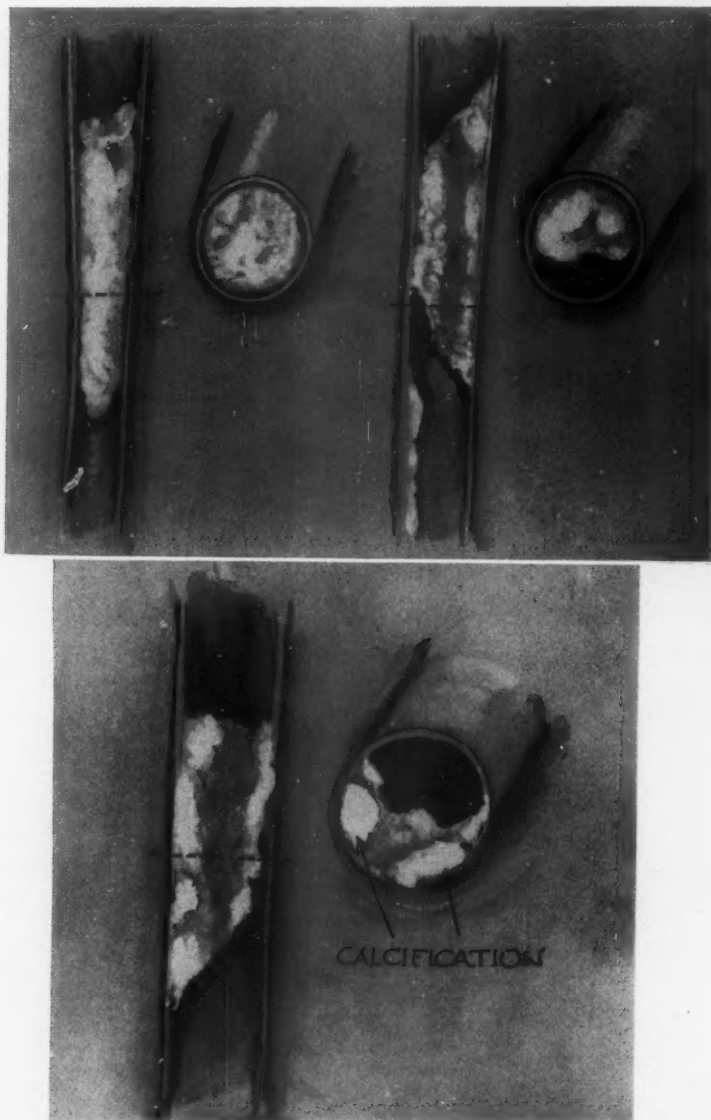

Fig. 3. Completely circumferential arteriosclerotic occlusive lesions (*upper left*) are usually readily removed with an intraluminal stripper since the occluding mass is only loosely adherent to the media. More commonly, the lesions are eccentric (*upper right*) and must be removed under direct vision since the relatively normal intima opposite the plaque separates with difficulty from the media. Where there is extensive calcification (*bottom*) the lesion extends into the media and use of a stripper may perforate the vessel wall.

artery distal to the graft (fig. 1). Although early failures may be attributed to inadequate "run off," late failures often result from inadequate "run in"; *i.e.*, the occlusive process proximal to the graft progresses to a point where blood flow into the graft is seriously curtailed (fig. 2). Compression of a graft from external force may cause occlusion and acute thrombosis. Finally, elongation of the graft due to disappearance of the pleats may produce angulation and reduction in size of the lumen.

Indications for operation for femoral popliteal occlusion are broader than those for aorto-iliac disease, primarily because operations upon the peripheral vessels are less exacting on the patient. In most instances low spinal anesthesia may be employed, and the involved vessels are accessible and easily controlled so that blood loss is not a significant factor. Therefore, restorative procedures are recommended at this level for relief of claudication, to promote healing of necrotic areas, and even to permit amputation at a lower level.

The choice of an operative procedure is based more upon the pathologic process itself than upon the extent of the disease (fig. 3). Thus, unless extensive calcification is present, thrombointimectomy usually can be done. It was formerly the opinion that a bypass procedure should be employed for the relief of ischemic symptoms in the presence of diffuse disease involving vessels distal to the popliteal artery, but with a residual lumen. However, it now appears that the use of a bypass graft under these circumstances may actually be harmful since the elimination of a pressure gradient across the occluded segment removes the stimulus for functioning of collateral circulation.

SUMMARY

1. Results of operations in 65 cases of occlusive peripheral vascular disease are summarized, with particular reference to late results following bypass grafts and thrombointimectomy.

2. In 24 cases of aorto-iliac occlusion, 14 were treated by grafting and 10 by thrombointimectomy. There were 2 early failures and 3 late failures in the patients treated with grafts. There were no failures in the group treated by thrombointimectomy.

3. In 41 cases of femoral popliteal occlusion, 26 were treated with grafts and 15 were treated by thrombointimectomy. Among the 26 patients treated with grafts there were 6 early failures and an additional 15 failures. Among 11 patients treated with thrombointimectomy, there were 4 early failures but no late failures.

4. Because of the frequency of late closure of bypass grafts, it is believed that thrombointimectomy is the preferable method of treatment in occlusive peripheral vascular disease.

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INTESTINAL ANTISEPSIS*

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Intestinal antisepsis, a relatively new addition to surgery of the colon, dates back only to the 1938 report of Garlock and Seley[11] on the use of sulfanilamide. Since that time intestinal antisepsis has been accepted in many areas as part of the routine preparation for colon surgery.

Evidence for the value of intestinal antisepsis has been provided by the experimental studies of Poth and associates[14] and Cohn and Rives[4, 9, 10] in which greater stability of colonic anastomoses was shown, when protected with antibiotics. Such evidence would be difficult if not impossible to obtain from clinical cases, and a statistic evaluation of the effect of antibiotics on the mortality and morbidity of colon surgery will probably require several more years of study of carefully controlled clinical cases. In the interim, experimental evidence plus clinical impressions warrant continued use of routine intestinal antisepsis for surgery of the colon.

If intestinal antiseptics are to be widely used, then certain criteria should be established for their evaluation. Poth's[13] nine criteria for the ideal agent have been compressed into three essential requirements for a useful intestinal antiseptic: (1) rapid, highly bactericidal activity against pathogenic organisms in the gastrointestinal tract; (2) ability to prevent development or overgrowth of pathogenic organisms; and (3) low toxicity, local as well as systemic, and limited absorption from the intestine. Acceptance of these criteria and of the experimental evidence for the value of intestinal antisepsis requires further scrutiny of three basic problems of intestinal antisepsis:

1. What is the relative efficacy of various antibacterial agents?
2. What is the clinical application of this information?
3. What are the dangers of intestinal antisepsis?

ANTIBACTERIAL AGENTS

In an effort to evaluate the relative efficacy of various agents, we have conducted a 4-year comparative study of all agents currently available for preoperative preparation of the colon.[5-8] Since the entire study has been conducted in a single institution using standardized techniques, comparisons between different drugs are easier than are such comparisons based upon studies of individual agents each evaluated in different institutions.

This study was conducted upon patients chosen from the surgical wards provided they had no known lesions of the colon. Results were periodically confirmed on patients who did have lesions in the colon.

For almost all of the drugs, we have employed a 72-hour period of preparation. Although others have advocated a 48- or even a 24-hour period of preparation, we believe that adequate mechanical cleansing is of the utmost importance and truly adequate cleansing cannot be obtained in 1 or even 2 days. Thus we advocate a full 3-day period of mechanical cleansing combined with antibiotics.

After the patients were selected, a control stool was obtained for quantitative bacteriologic analysis and the patients were placed upon a low residue diet, were given a cathartic, were placed upon daily enemas, and were given the antibiotic of choice. Stools were collected each day during therapy and for several days after therapy and all

TABLE 1
Classification of intestinal antiseptics

Not recommended

Chloramphenicol (Chloromycetin)
Chlorquinaldol (Sterosan)
Erythromycin
Furazolidone (Furoxone)
Novobiocin (Albamycin, Cathomycin)
Penicillin V
Ristocetin (Spontin)
Sulfasuxidine
Sulfathalidine
Tetracyclines
  Chlortetracycline (Aureomycin)
  Oxytetracycline (Terramycin)
  Tetracycline (Achromycin)
  Tetracycline V
Tetracycline-Nystatin (Mysteclin)
Thiostrepton

Intermediate

Neomycin
Chlorquinaldol-neomycin
Oxytetracycline-neomycin (Enterobiotic)

Recommended

Special use:
  Erythromycin-neomycin
  Novobiocin-neomycin
  Ristocetin-neomycin
  Tetracycline-neomycin
General use:
  Amphotericin-neomycin
  Bacitracin-neomycin
  Kanamycin
  Nystatin-neomycin
  Polymyxin B-neomycin
  Su fathalidine-neomycin
  Thiostrepton-neomycin

stools were subjected to quantitative aerobic and anaerobic bacteriologic analysis.

On the basis of a study of 30 agents, the drugs have been divided into three major groups: not recommended, intermediate, and recommended (table 1).

Not recommended. In the group of drugs that are not recommended are 16 agents. Each failed to control the bacterial flora of the stool and several produced so many side reactions as to make them undesirable on this basis alone. In addition, most of these agents are readily absorbed from the gastrointestinal tract which means that their maximal activity will not be exerted in the colon. Rapid absorption and wide use for other conditions suggest that the patient may have already been exposed to this drug

and may have, or readily develop, organisms resistant to this particular agent.

Several agents in this group deserve a special word: Clorpactin WCS 90, the sulfonamides, and the tetracyclines. Clorpactin WCS 90 is the only agent which was not studied clinically but the form of therapy required for this agent[3, 12] made us feel that an adequate study could best be conducted in the experimental laboratory. Clorpactin WCS 90 provides good control of the bacterial flora in the washings immediately following irrigation, but swabs of the mucosa following irrigation still contain a relatively normal bacterial flora. When intestinal contents pass over the bowel there will no longer be any antibacterial effect since the agent is inactivated by contact with organic material. This problem, the inability to use the drug preoperatively, and the undue contamination that must accompany the copious irrigations required at the time of operation combine to make Clorpactin WCS 90 unsatisfactory for intestinal antisepsis.

Neither Sulfasuxidine nor Sulfathalidine provided satisfactory reduction of the bacterial count of the feces and therefore these agents should not be used.

We have tested Aureomycin, Terramycin, Achromycin, and tetracycline V and none of these provide adequate control of the bacterial flora of the colon.

Intermediate. A group of three drugs provide better control of the bacterial flora than do the drugs in the unsatisfactory group but are still not quite good enough to be highly recommended. Neomycin is the only *single* agent in this chart and with the exception of one other drug, it will be a component of every combination to be discussed from this point on.

Recommended. The recommended drugs have been subdivided into those recommended for special purposes and those for general use. Control of the bacterial flora is approximately the same for all drugs in this group and the incidence of side reactions is negligible for the entire group but there are other differences which make this subdivision worthwhile.

The drugs recommended for special use are combinations of neomycin with various drugs widely used for systemic therapy. All are readily absorbed from the gastrointestinal tract and, with the exception of ristocetin, all are commonly administered by the oral route. Since these drugs are widely used it is likely that organisms re-

sistant to these antibiotics will already be present in the hospital population. Three of these drugs are specifically indicated in the treatment of staphylococcal infections. Utilization of these combinations for routine preparation would unquestionably lead to the more rapid development of resistant staphylococci and thereby make these drugs lose their most outstanding property.

Specific indications for each of these agents are: (1) for the treatment of any patient who develops a staphylococcal infection of the gastrointestinal tract, (2) for the preoperative preparation of any patient who has already been on prolonged antibacterial therapy for some other purpose and therefore might be expected to develop resistant organisms in the gastrointestinal tract, or (3) for the treatment of a postoperative or postantibiotic diarrhea.

In contrast to the group just discussed are seven agents which can be highly recommended for general use. All except one are combinations of neomycin with some other poorly absorbed antibacterial agent. The majority are not widely used for other purposes, which lessens the likelihood of the development of resistant forms. The poor absorption from the gastrointestinal tract provides a maximum antibacterial level in the colon where it is most needed. Disturbing side reactions are at a minimum. The control of the bacterial flora of the stool is excellent with any drug in this group.

There are two combinations of neomycin with antifungal agents; Amphotericin-neomycin and Nystatin-neomycin. Both provide superior control of the bacterial flora and also prevent the outgrowth of yeast forms during the period of preparation. For those who believe that such postoperative complications as stomatitis, thrush, diarrhea and other monilial problems are to be avoided at all costs, the choice of one or the other of these combinations would be ideal. In our experience the only place where antifungals have been found essential has been in the preoperative preparation of infants to obviate the development of thrush.

There are four drug combinations which perhaps show a slight superiority in the control of the bacterial flora of the feces. These four are: Bacitracin-neomycin, Polymyxin B-neomycin, Sulfathalidine-neomycin, and Thiostrepton-neomycin.

Recently we have studied Kanamycin, a new drug having many properties similar to neomycin.[1] Our experience to date indicates that this

is the best *single* agent so far evaluated. We have not noted any side reactions and the absence of diarrhea is one feature which distinguishes it from neomycin. There is almost no absorption from the gastrointestinal tract as measured by blood levels and as determined by the extremely high stool levels. The lack of absorption from the gastrointestinal tract will unquestionably lower the frequency with which it is used in general practice and this should be of value in lowering the incidence of resistant organisms in the gastrointestinal tract. More recently we have also been impressed by the absence of either local or systemic reactions following intraperitoneal injection of Kanamycin.[3] This is in contrast to our experience with both tetracycline and neomycin.

CLINICAL EXPERIENCE

Beginning in July 1955, all colon cases on the Louisiana State University Surgical Service at Charity Hospital in New Orleans have been treated by a standardized means of antibiotic therapy. A program was instituted using tetracycline (Achromycin) and neomycin since this was the most effective drug studied up to that time.

On the basis of our experimental experience,[4, 9, 10] antibiotic therapy was divided into three phases. The first phase was preoperative

TABLE 2
Clinical study of 275 patients treated with various phases of antibiotic therapy

Type of Therapy	Cases	Description
Preoperative	230	Achromycin (200 mg.) + neomycin (1.0 gm.) Given q.h. for 4 hr.; then q.i.d. for 3 days
Operative	100	Achromycin (250 mg.) + neomycin (1.25 gm.)
Postoperative	83	Achromycin (150 mg.) + neomycin (750 mg.) Given t.i.d. for 5 days
Preoperative, operative and postoperative	52	

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preparation. The second phase was the intra-luminal instillation of an antibiotic powder. The third phase involved the postoperative instillation of antibiotics through a plastic tube inserted in the colon. In the first 3 years, 275 patients were treated with various parts of this program (table 2).

The largest single group included the 230 patients prepared with Achromycin-neomycin for all of the usual colon procedures in adults and infants, and a number of procedures that ultimately did not involve the colon, but in which the colon appeared to be implicated by preoperative studies (table 3). There were relatively few side reactions to this form of preparation, and only 3 patients had to have therapy discontinued because of disturbing side effects during preparation (table 4). We have been fortunate in not observing a single case of enterocolitis in relation to antibiotic preparation.

Antibiotic powder was placed in the colon at the time of surgery in 100 patients, and antibiotics were injected through the tube in the postoperative period in 83 patients (table 3). There were no complications which could be unquestionably attributed to the use of the tube, except for the patients who received intra-peritoneal antibiotics after the tube came out of the bowel. Before the use of Kanamycin we objected to the intraperitoneal administration of antibiotics because this caused pain in unan-esthetized patients in our experience, and experi-mental work indicates it may well be the cause of other complications. When therapy is completed the tube is simply removed. No complications have resulted from the removal of this tube. There have been several occasions when the tube has been credited with saving a patient's life, and for this reason we believe that further use of postoperative intraluminal antibiotics is justified.

The greatest interest lies in the 52 patients who received all three phases of antibiotic therapy. Study of these cases suggests that they have fared better than similar cases not treated with antibiotics. The triple form of therapy appears to be worthwhile and is still under study. The instillation of surgical powder at operation and the use of the plastic tube to instill antibiotics into the lumen of the bowel in the immediate postoperative period should be of particular value in patients operated upon for emergency purposes following trauma to the colon or subsequent to obstruction of the colon. The reaction surround-ing the operative area should be decreased by

TABLE 3

Antibiotic therapy in 275 patients subjected to various operative procedures, July 1, 1955, to June 30, 1958

Procedures	Preoperative Therapy	Operative Therapy	Postoperative Therapy	Preoperative, Operative, and Postoperative
Primary anastomosis...............	107	75	70	45
Colostomy..........	65	20	6	4
Colotomy...........	8	5	7	3
Colon not opened...	50			
Totals............	230	100	83	52

TABLE 4

Side effects in 230 patients treated with preoperative Achromycin-neomycin preparation

Type of Reaction	No. of Reactions	No. of Patients
Nausea.......................	33	
Vomiting....................	21	
Diarrhea...	10	50
Cramps......................	5	
None........................		180
Totals......................	69	230

adequate control of the bacterial flora within the lumen of the colon. Such control can be obtained with intraluminal antibiotics but cannot be achieved with parenteral antibiotics nor sustained by antibiotics administered only during the pre-operative period. However, no form of antibiotic therapy can be utilized as a substitute for properly performed surgery.

DANGERS OF INTESTINAL ANTISEPSIS

As intestinal antisepsis came into wider general use, the dangers of severe colitis or enterocolitis as a result of yeast complications were suggested. Even though some of the effective intestinal antiseptics do permit the outgrowth of yeasts, these yeasts are frequently not pathogenic, and there is little proof that the yeasts themselves are the cause of complications, except in infants who develop thrush. Except for infants, we have not been impressed by the importance of yeast complications nor with the necessity of routinely using an antifungal agent in the preoperative preparation of the colon.

The emergence of antibiotic-resistant staphylococcal diarrhea has caused some to abstain from the use of intestinal antiseptics. Enterocolitis has been reported in the literature more frequently since broad spectrum antibiotics came into use, but this entity was described before the advent of antibiotics and its development in some cases where antibiotics have been used either for very brief periods or not at all would indicate that broad spectrum antibiotics are not the only causative agent for this disease. We do not believe that the occurrence of a staphylococcal diarrhea in an occasional patient is sufficiently dangerous to warrant cessation of preoperative intestinal antisepsis for surgery of the colon, particularly since some effective antistaphylococcal drugs are available if they are not abused.

If antibiotics are used to permit violation of sound surgical principles, then antibiotics are being erroneously used and are possibly dangerous. Recent articles dealing with the use of antibiotics for the resection and primary anastomosis of an acutely obstructed colonic lesion suggest that antibiotics are being misused in this connection. Much of the writing on this subject fails to distinguish between obstruction of the right and left colon. Resection of an acutely obstructed right colon was performed with safety in many centers before the advent of antibiotics, and no one would argue with this form of therapy today. But the primary resection and anastomosis of an obstructed left colon without some proximal decompression should still be practiced only with considerable caution. It is probably true that such procedures are safer than they were in the pre-antibiotic days, but this does not mean that such procedures are sufficiently safe to use routinely, and there is as yet little evidence to indicate that such procedures are safe at all. On the contrary, there is evidence that such procedures are unduly dangerous and should be abandoned. Experimental work[2] has indicated that animals with a colonic obstruction can be decompressed by colostomy with no mortality, but that a primary resection and anastomosis, even with antibiotic protection, is associated with a mortality of 40 to 70 per cent. This markedly increased risk does not seem justified in patients when it is well established that a colostomy can be performed with such a low risk.

A final possible disadvantage to the use of intestinal antiseptics would be the possibility that intestinal antisepsis might increase the spread of tumor cells. Vink[15] suggested such a possibility on the basis of some experimental work in the rabbit, but this work has not received the attention it deserves. In attempting to repeat this work, we too have been impressed by the apparently increased rate of tumor metastases in the presence of intestinal antisepsis. Such a study requires a large number of experiments to be statistically valid, but work to date suggests that there is a greater growth of tumor cells in those animals that have been treated with antibiotics than in those not so treated. If this is confirmed statistically, then some search must be made for an agent that will hinder this type of tumor spread without at the same time interfering with the beneficial effects of control of the bacterial flora.

The real and possible dangers of intestinal antisepsis have been discussed and must be weighed against its advantages. The control of the bacterial flora of the colon with its attendant decrease in risk of peritonitis, fistula formation and wound infection, and with the well documented improvement in healing of a colon anastomosis, all argue forcefully for the continued routine use of preoperative intestinal antisepsis for surgery of the colon.

SUMMARY

1. The criteria for an ideal intestinal antiseptic have been outlined.

2. A survey of 30 different antibiotics has permitted a classification of intestinal antiseptics into those which are not suitable and those which can be recommended.

3. The drugs most highly recommended for intestinal antisepsis are poorly absorbed from the gastrointestinal tract and maintain activity in the colon without producing a significant number of undesirable gastrointestinal side effects.

4. An experience of three years with a triphasic program of antibiotic therapy has convinced us of the value of these forms of therapy.

5. The possible disadvantages of intestinal antisepsis have been enumerated and it has been suggested that the advantages of this form of therapy outweigh the possible disadvantages.

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MECHANISMS AND PREVENTIVE MEASURES IN DISSEMINATION OF CANCER*

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The problems involved in the dissemination of cancer are complicated; there are numerous factors and mechanisms, many of which are poorly understood.

FACTORS IMPORTANT IN DISSEMINATION OF CANCER

The factors influencing the spread of cancer are extremely varied. Some are no doubt dependent upon each other. A brief description of some of them may be helpful.

Invasive Property of Cancer Cells

This characteristic, which to a great extent controls the rapidity of growth of the tumor, is dependent on numerous factors a few of which will be described briefly below.

Power of progressive multiplication of cells. It is well known that tumors vary greatly in their rapidity of growth, and that some grow more rapidly at certain times than others. Also, it is a well known clinical fact that some tumors metastasize slowly whereas others metastasize rapidly. The variation in the time required for metastases to develop following resection of a tumor is particularly related to the power of progressive multiplication. On occasions, the microscopic nests of cells which escaped before or during the operation seem to lie dormant for years. We agree with Hadfield[17] that if more than 2 years elapse between the time of operation and development of metastases there is probably a dormant period during which the cells are not proliferating; or if so, very slowly. As will be discussed later, it is our contention that during this dormant phase when either their invasive quality is subdued, or resistance of the host increased, these cells might be destroyed by some mechanism (*i.e.*, anticancer agents) now available.

Motility of cancer cells. Enterline and Coman[11] have reported the migration of cancer cells at rates as high as 414 μ per minute. This ameboid type of motility would influence to a certain extent the speed of local growth of a tumor by contiguity and by tissue planes. Movement of cancer cells by the lymph and vascular stream is of course much faster, but not necessarily related to any activity of the cell itself; metastases develop by these means.

Elaboration of toxic or lytic substances. This factor has been discussed for decades, but there is no agreement as to its importance. The fibroblastic reaction around a tumor may be the result of elaboration of tumor metabolism; one of the best examples of this reaction is the dense connective tissue found associated with a scirrhous carcinoma of the breast.

Cellular mitosis. The various phases of mitosis are described as interphase, prophase, metaphase, anaphase and telaphase. The interphase, or resting phase, extends over a much longer time (10 to 18 hours) than all the stages of mitosis combined. Lewis[22] reports the metaphase of malignant cells in tissue culture to be 12 to 50 minutes, compared to $3\frac{1}{2}$ to 12 minutes for normal cells. On the contrary, the interphase or resting phase is apt to be much shorter in cancer cells than in normal cells.

Hormones. In a small number of tumors (*e.g.*, carcinoma of the breast and prostate) the growth of the tumor is dependent upon hormones. For example, Huggins and Dao[18a, 18b] have shown that many patients with carcinoma of the prostate will benefit from castration and estrogen hormones, and many female patients with cancer of the breast will benefit from castration and male hormones. About one-half the carcinomas of these two organs are hormone dependent, meaning that the other one-half will not benefit from the therapy just described. The benefit, in these tumors, from adrenalectomy and hypophysectomy is of the same type.

Nutrition. In certain animals it has been shown that restriction of the caloric intake[30a, 30b] will decrease the genesis of tumors, *i.e.*, the incidence

of tumor formation will be decreased, and the time of appearance delayed. This nutritional status apparently exerts a slight role in human cancer since vital statistics indicate that the death rate from cancer in obese people is higher than that in thin people.

Virulence of tumor and resistance of host. During recent years we have been increasingly aware of the role of virulence of the tumor and resistance of the host in the growth of tumors. It would seem that a decreased resistance of the host to tumor formation is actually responsible for the development of the tumor itself. It is barely possible that virulence of the tumor is nonexistent, and is dependent entirely upon host resistance.

The importance of these two factors is emphasized by the report of Rich (*cf.* Franks[14]) in which carcinoma was found, at autopsy, in 14 per cent of men past the age of 50. This incidence is much higher than the clinical incidence of cancer of the prostate, indicating that the majority of these carcinomas remain local and do not metastasize. In some mysterious way (perhaps by way of host resistance) these carcinomas do not develop the invasive characteristics possessed by the tumor observed clinically. This high incidence of carcinoma of the prostate at autopsy has been confirmed by other pathologists.

MECHANISMS OF THE SPREAD OF CANCER

There are four major mechanisms by which cancer spreads: (1) by contiguity in tissue planes, (2) by way of the lymphatics, (3) by implantation, and (4) by vascular channels. Spread by contiguity in tissue planes is a characteristic mechanism displayed by practically all malignant tumors. Spread by the lymphatics is common and has been studied in detail by numerous investigators. Accordingly, in this presentation we are confining our discussion to the two latter mechanisms, namely, implantation and vascular channels.

Dissemination by Implantation

For years it has been known that cells may be displaced by operation or diagnostic manipulation such as needle aspiration, but inadequate attention has been paid to these mechanisms of spread. Perhaps the first physician to emphasize this mechanism of spread was the British surgeon Ryall.[27a, 27b] He reported 25 examples of implantation; 16 of these were in the wound after resection of the cancer. In 5 patients cancer grew

FIG. 1. Recurrence in the scar line in a patient having a radical mastectomy. The nodule was first observed 3 years after operation. This appears to be an implantation, at the time of operation.

into the tract made by the needle sewing up the wound. In one case cells grew out along the tract made by the needle following a paracentesis for ascites. Zelman[32] has reported the growth of tumor out along the needle tract following aspiration. It was excised and another nodule was found just under the fascia. Both specimens revealed adenocarcinoma similar to the cells encountered in the original specimen at the time the Miles' operation was performed.

Ackerman and Wheat[1] have reported several types of implantation. In one of their cases there was a cancer implant in the skin graft following a radical mastectomy. In another the cancer grew out along the needle tract after an aspiration biopsy. Two or three others represented implants in the wound following resection for intraabdominal cancer. Perhaps the most unique type of implantation is that reported by Beahrs and associates[4] who observed the development of carcinoma in the hemorrhoidectomy wound in 3 patients following hemorrhoidectomy. In these patients symptoms of a carcinoma of the colon or rectum were present before the hemorrhoidectomy was performed. In a 4th patient who had carcinoma of the colon, an adenocarcinoma was found in the ulcerating surface of a hemorrhoid, apparently representing a frank implant on the ulcerated area of the hemorrhoid. LeQuesne and Thomson[20] also reported the implantation of malignant cells into a fresh hemorrhoidectomy
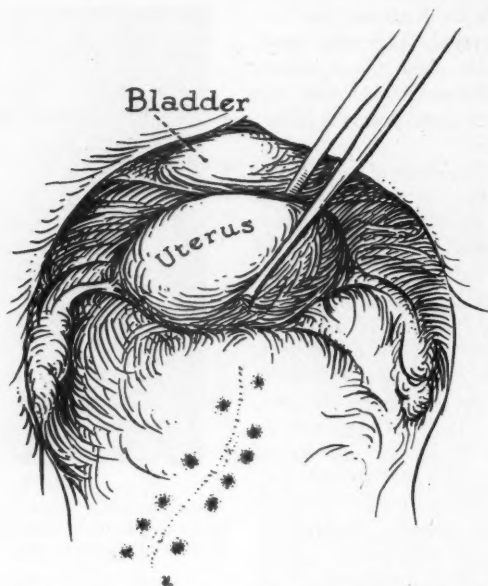
Fig. 2. This patient had a Miles' operation for carcinoma of the rectum 18 months ago; 5 months later she had an operation to revise her colostomy. At this operation, numerous small peritoneal implants were noted on the peritoneum of the lower abdomen, but more dramatic were the small implants in the peritoneum of the pelvic floor, at points where the needle had penetrated during its closure. (From Cole and associates, Bull. New York Acad. Med., *34:* 163, 1958.)

scar from a tumor in the bowel. In another patient they noted an implant of the perineal wound following resection of a carcinoma of the rectum. Recurrence in the scar line of patients having a radical mastectomy is not uncommon, and on most occasions appears to be due to implantation at the time of operation (fig. 1).

Bush[7] has reported the development of a malignant nodule at the site of the needle puncture 2 months after abdominal paracentesis in a patient who had ascites caused by metastatic adenocarcinoma of the ovary. In another case he reports an implant in the abdominal wound 3 months following extensive resection of a carcinoma of the pylorus; in still another case, he reports a malignant nodule in the scar resulting from closure of a loop colostomy made after resection of the left colon for carcinoma.

All surgeons and pathologists are familiar with dissemination into the pleural and abdominal cavity. In the pleural space the implants originate from a primary or secondary tumor of the lung. In the abdominal cavity they may arise from any of numerous tumors within the abdominal cavity. Surgeons are too familiar, indeed,

with the innumerable peritoneal implants encountered frequently when operating on patients with carcinoma of the stomach, or colon. Operative manipulation no doubt tends to give rise to these implants unless careful precautions are taken to prevent them; especially when the tumor has eroded through the peritoneal surface (fig. 2).

Implantation of cells at anastomotic line following resection of colon. Several years ago three different groups,[9a, 15, 24] including the senior author, independently became alarmed about the large number of recurrences in the suture line following resection of the colon. We found recurrences in the suture line in about 10 per cent of our series and in a majority of them it seemed that implantation was the most likely explanation. The other two groups arrived at the same conclusion. The credit should go to Morgan and Lloyd-Davies[24] for first calling attention to this possible mechanism of implantation. Since then, numerous authors have commented on this complication. There is ample evidence that in at least a certain portion of these cases the recurrence does occur at the suture line since a large number of authors

FIG. 3. The silk suture (*S*) just beneath the carcinoma recurring near the suture line indicates the recurrent nodule is in the suture line.

have reported finding silk sutures in the tumor area[1, 13, 20, 23, 25] (fig. 3). Other surgeons[2, 13, 20] have cited implantation as a likely cause of recurrence at the suture line following resection of the colon.

Spread by Vascular Channels

During the past several years numerous articles have appeared in the medical literature calling attention to the erosion of veins by tumor thus creating the possibility of venous emboli of cancer cells. The incidence of venous ulceration varies largely between 20 and 40 per cent, although Brown and Warren[5] report that in their series of cases venous invasion was noted in 61 per cent. The high incidence of venous invasion in their series is presumably explained on the basis that these data were obtained from autopsies. Grinnell[16] reports an incidence of venous invasion in 36 per cent of patients with rectal carcinoma and in 33 per cent of patients with carcinoma of the colon. In Grinnell's series the 5-year survival rate was 37 per cent in the patients with venous invasion, contrasted to 76 per cent in the patients without venous invasion. Barringer and

associates[3] conducted a study in which they injected the veins in the resected specimens of colonic carcinoma with an opaque medium (warm Bromionol), and took x-rays. This study revealed, by x-ray, venous occlusion in 51 per cent of cases and, by microscopic examination, 38 per cent venous invasion. Still more recently, Collier and associates[10] studied 218 patients having resection of the lung for carcinoma. Of this series, 100 had been observed for more than 5 years. They noted that in the patients with vascular invasion the 5-year survival rate was only 6 per cent, whereas in those without vascular invasion it was 75 per cent. If no vascular invasion or positive nodes were found, the 5-year survival rate was 83 per cent.

In 1953 we conducted some experiments perfusing resected specimens containing carcinoma of the colon or rectum and examined the venous return for malignant cells. We reported[9] finding malignant cells in carcinoma of the rectum (fig. 4) and because of this, began the procedure of primary ligation of the vascular trunks supplying the tumor area, before operative manipulation was begun. In the first 100 patients in whom we[26] searched the peripheral blood as well as deep venous trunks, for cancer cells, we found cancer cells (figs. 5*A* and 5*B*) in the blood in 17 per cent of patients with operable tumors, and in 31 per cent of patients with inoperable tumors. In unpublished data concerning an additional 270 cases the percentage remains about the same, although it is higher in recent cases in which we changed our technique to one utilizing Streptolysin. We do not yet know the significance of these cells, although many of the patients who had cells in the blood before or during the operation are already dead. Many others show no evidence of recurrence, but in this group less than 1 year has elapsed since the observation; they may have living metastatic deposits which may not reveal real invasive tendencies for years. On several occasions we have noted a shower of cancer cells during operative manipulation.

In 1955 Engell[11] reported finding cancer cells in the blood draining from the tumor in 54 per cent of 76 patients with cancer of the rectum and in 70 per cent of 31 patients with cancer of the colon. Engell found cells in 35 per cent of patients with grade II tumors; in 78 per cent of patients with grade III tumors; and in 100 per cent of patients with grade IV tumors.
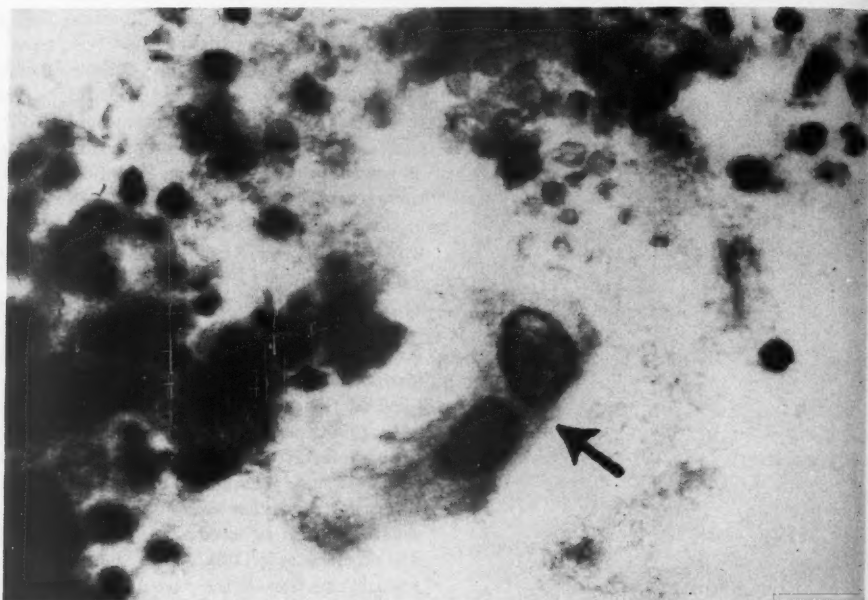
Fig. 4. Malignant cells (*arrow*) in stained smear obtained by centrifuging blood and saline perfused through the vessels supplying a carcinoma of the rectum removed at operation. (From Cole, W. H., Packard, D., and Southwick, H. W., J. A. M. A., *155:* 1549, 1954.)
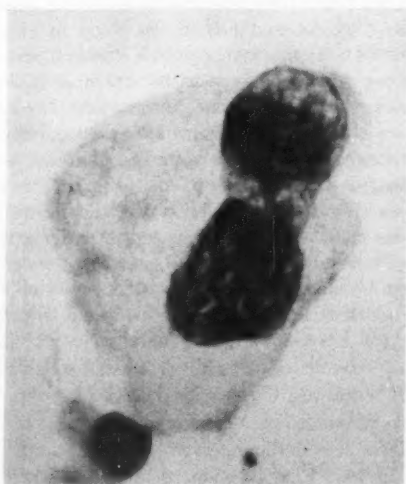

Fig. 5A. Tumor cell isolated from the inferior vena cava of a patient undergoing a hysterectomy for sarcoma of the uterus. Papanicolaou stain ($\times$ 1900).

Fig. 5B. Cancer cells from the antecubital vein of a patient with far advanced epidermoid carcinoma of the tongue. Papanicolaou stain ($\times$ 1900).

ROLE OF STRESS IN EXPERIMENTAL DEVELOPMENT OF CANCER

Years ago the senior author did a radical mastectomy on a patient with carcinoma of the breast and noted a very rapid metastatic spread of the disease thereafter. The tumor had been present for about 9 months. At operation, nodes were attached to the axillary vessels and required

considerable dissection for removal. In retrospect it was rather obvious that a cure could not be expected. Within 6 weeks the patient was complaining of pain in the pelvis and back. X-rays taken a few days later revealed metastases in the lungs and pelvic bones. The patient died 6 weeks later, with extensive metastases. It actually appeared that the operation activated the tumor and made it much more invasive. Almost all surgeons have seen examples of rapid dissemination of cancer following operation, suggesting that the operation may have been a factor in the increased growth.

In an effort to find out if trauma would increase pulmonary metastasis, Lewis[21] conducted some experiments in our laboratory utilizing the T-241 tumor and C57 Bl/6 mice. Lewis made a sterile suspension of tumor cells and injected 100,000 cells into the hind foot of each of a group of mice. On the 22nd day after inoculation, and past the time when it is known that cells have disseminated from the primary tumor, the extremity bearing the tumor was amputated in one-half of the animals. Pulmonary metastases were observed in 57 per cent of 56 control animals, and in 96 per cent of 68 animals having amputation of the tumor bearing extremity. This result could be interpreted in one of two different ways. One interpretation might imply that the operation itself had reduced the resistance of the animal to the cancer cells growing in his foot. The other explanation would be dependent upon the possibility that the tumor was exerting an inhibitory effect on formation and growth of metastases, and its removal thereby allowed the metastases to grow faster and develop in greater numbers. This latter explanation was the one offered by Schatten,[23] who was conducting a similar study simultaneously on S-91 and DBA 49 tumors in mice. In another series of experiments by Schatten and Lewis, performed independently, amputation of the normal leg did not result in an increase of pulmonary metastases.

In an effort to obtain more data on the possible role of trauma in the decrease of host resistance, Buinauskas[6] conducted some experiments in our laboratory inoculating white female Holtzman rats subcutaneously with Walker 256 cells and performing a celiotomy in one-half of the animals. Of 85 inoculated animals having celiotomy at the same time, "takes" were observed in 61.1 per cent in contrast to "takes" in 31.6 per cent of 79 control animals not having celiotomy. These experiments would appear to indicate rather clearly that the stress of trauma was the vital factor in the increase in "takes." All animals were observed for 90 days or until their death. In general the control animals with tumors lived longer than the animals subjected to celiotomy.

In an effort to obtain data on this problem from a different type of experiment. Chan and associates[8] of our laboratory conducted some experiments in which they damaged the liver in Holtzman white rats with carbon tetrachloride by daily administration of the drug for 4 days preceding the intraportal inoculation of 25,000 Walker 256 cells aged for 12 hours to decrease the "take" below 100 per cent. In 70 rats receiving carbon tetrachloride, the incidence of "takes" was 42 per cent; in 70 controls not receiving carbon tetrachloride, the incidence of "takes" was 18 per cent. Both of these groups had the operative stress of celiotomy before inoculation of the tumor cells, but only one group had the added stress of carbon tetrachloride. These experiments indicate that chemical stress or the liver damage lowered the resistance of the host to tumor cells. As stated previously, numerous surgeons have observed a rather explosive development of metastases after an operation. For example, Jackson and associates[19] report the death of a patient having resection of the colon for carcinoma in ulcerative colitis within 6 weeks after the operation. Since there was no gross evidence of metastatic spread at the time of operation, development of fatal metastases in this short period of time is highly suggestive that the operation itself might have been a factor in increasing the spread.

The fact that operative and chemical trauma in animals appears to decrease the resistance of the animal to cancer cells, and the fact that, occasionally, cancer spreads rapidly and wildly after operation does not deter us in our conclusion that surgical treatment of cancer is the best therapeutic mechanism available. We already know what surgery will do for cancer. For example, the 5-year survival rate following resection for carcinoma of the breast, colon, rectum, and many other tumors is as high as 50 per cent. If we could find some mechanism which might neutralize the deleterious effect of trauma (if existent) on the resistance of the host to tumor cells, we might improve the ultimate results considerably. However, we wish to emphasize that as yet we have no proof that operative trauma decreases the resistance of the human patient to his cancer cells. Nevertheless, there is strong circumstantial evidence that this may be true.

PREVENTION OF SPREAD OF CANCER

Numerous mechanisms can be carried out to minimize the possible spread of cancer incident to operation.

Preparation of skin in the operating room. The authors wish to emphasize very strongly that when the skin is prepared for operation a precautionary measure must be taken not to massage or traumatize the tumor area, particularly if the mass is in an exposed position and palpable. Soap and water preparation has been accepted rather widely for preparing the skin preceding operation, but in this preparation much massage of the area is obviously carried out by the scrubbing process. It is our recommendation that when the tumor is palpable and possibly malignant, soap and water must not be used in preparation of the skin. Instead, some antiseptic should be painted on the skin.

Tyzzer[31] showed that massage of a mouse tumor increases the tendency for spread and development of pulmonary metastases. He reported that in the animals not having massage, pulmonary metastases were not found earlier than the 39th day after subcutaneous inoculation of the tumor. However, in mice having massage of the tumor 80 per cent had visible pulmonary metastases by the 36th day after inoculation.

Careful handling of tissue during operation. We hope that all surgeons are very cautious in handling the tumor during its resection regardless of the site or type. Since metastases by way of the lymphatics or by way of the blood stream might be increased by manipulation of the tumor incident to its removal, there seems to be ample reason to pay particular attention to this precaution. The surgeon obviously wants to remove as much normal tissue adjacent to the tumor as possible so that he can prevent manipulation of the tumor and minimize cutting the lymphatic and venous channels which might contain malignant cells. It would appear that trauma to the tumor might spread it by the lymphatics or the vascular route.

Prevention of implantation of cancer at suture line following resection of colon for cancer. Reference has already been made to the possible role of implantation of cancer cells as a cause of recurrence in the suture line following resection of colonic carcinoma. To prevent possible implantation we utilize two precautions. In the first place, we ligate the lumen of the bowel several inches above and below the tumor just as soon as we determine operability and before operative manipulation is begun. We discovered that ligation of the lumen, which obviously took place at least 2 hours before examination of the specimen in the surgical pathology room, seemed to eliminate cells from the lumen outside the ligatures. For example, smears taken inside the ligatures proximal to the tumor were positive in 42 per cent of cases whereas smears taken inside the ligatures distal to the tumor were positive in 65 per cent of cases. However, smears taken outside the ligatures were negative for cancer cells indicating that during the period of 2 hours following ligation of the lumen the cells which might have existed outside the ligatures at the beginning of the operation had now disintegrated and were presumably dead. However, as an added precaution we irrigate the two ends of the bowel with full strength Dakin's solution or 1 per cent Clorpactin XCB just before the anastomosis is performed. As an additional precaution, just after irrigation of the two ends, we excise an additional thin segment of the end of the bowel to eliminate any cells which might have been forced into the wall of the bowel when the crushing clamp was applied. Morgan and Lloyd-Davies[24] as well as Goligher and associates[15] irrigate or swab out the lumen of the bowel with 1-500 bichloride of mercury before anastomotic sutures are placed.

Ligation of vascular trunks leading to and from tumor area before operative manipulation is begun. When our investigation[9] in 1953 revealed cancer cells in the venous blood we immediately adopted the technique of ligating the vascular trunks leading to and from the tumor area. This can best be accomplished with tumors of the right colon, the transverse, and with less effect, tumors of the left colon and stomach. It is not possible with tumors of the rectum except to ligate the superior rectal vessels. Ligation of the major trunks would appear to cut down the major portion of the blood flow, although it would not eliminate the entire flow to and from the segment of bowel involved.

PROPHYLACTIC AND ADJUVANT THERAPY FOR CANCER

When we obtained favorable results from our animal experiments, indicating that the use of nitrogen mustard and triethylenephosphoramide at the time of inoculation of Walker 256 tumor

cells into the portal system of rats would sharply diminish the incidence of "takes," we began the use of this procedure in patients. A formal series was initiated in March 1956 including carcinoma of the breast, colon, rectum and stomach. Recently, we joined the adjuvant group of the National Cancer Institute with our patients having carcinoma of the stomach and lung.

In order to protect the patient, we have adopted certain prophylactic measures which we believe render the procedure safe even though we are dealing with very toxic drugs. We exclude all patients past the age of 70 from our formal series. To prevent an overdose in obese people, we do not give more than 30 mg. of nitrogen mustard for a course even though the patient's weight would indicate a much higher dose. Utilizing a course dose of 0.4 mg. per kg. of body weight, underweight patients will of course get less than 30 mg. For carcinoma of the colon and rectum, we give 0.1 mg. per kg. (maximum of 7.5 mg.) into a branch of the portal vein at the end of the operation; 0.1 mg. per kg. (maximum of 7.5 mg.) is diluted with 400 cc. of physiologic saline and left in the peritoneal cavity after the last suture is tied. On the next day the patient receives 0.1 mg. per kg. (maximum of 7.5 mg.) through a superficial vein and a similar dose the following day.

Patients with cancer of the breast are given ⅓ the course dose or 0.2 mg. per kg. (maximum of 15 mg.) through a superficial vein at the termination of the operation. On the first day after operation they are given 0.1 mg. per kg. (maximum of 7.5 mg.) through a superficial vein and a similar dose on the following day.

We now have approximately 130 patients in our series. Of these, 70 are patients with cancer of the breast and the remainder with cancer of the colon and rectum. We have had 2 operative deaths in the entire series; 1 occurring in a control patient with carcinoma of the colon, and 1 occurring in a treated patient with carcinoma of the colon. Accordingly, the number of operative deaths does not appear to be any greater than expected. There has been a slight increase in the amount of complications, including wound infection and seroma, but there have been no instances of frank wound dehiscence.

Insufficient time has elapsed in this formal series to determine the effects of this prophylactic or adjuvant therapy. However, in the patients with carcinoma of the breast the data look very encouraging, indeed. There are not enough recurrences in the patients with carcinoma of the colon and rectum to determine even a trend.

In all of the patients in our own series, we are repeating the dose every 4 months if the patient shows no evidence of bone marrow depression. No patient with a white count of less than 5000 is given the drug. Only a few of the patients are able to take more than three courses. We do not continue it beyond 2 years even though the patient's bone marrow might be within normal limits. We are quite sure, but have no proof, that a large part of the apparent good results in our breast series is due to the multiple doses.

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ADVANCES MADE IN CANCER RESEARCH

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Spending a few days at Miami Beach is always a pleasant experience, and I am told that Floridians consider March the best time of the year for a visit to this beautiful resort. For a much more pertinent reason, however, I am very glad to be here. It is a great privilege for me to participate in the excellent program of this meeting of the Southeastern Surgical Congress.

My assignment to discuss advances in cancer research has given me a most welcome opportunity to take stock, as it were; to reflect on the status of this complex segment of medical research, which I have no doubt will some day not only produce the means for the ultimate conquest of malignant diseases but also reveal some of the secrets of life itself.

It seems to me that a true perspective of the situation depends on the recognition that progress is measured by achievements in two separate and at the same time interdependent components of cancer research: resources and products. At the present time, I believe that it would not be extravagant to suggest that in both of its component parts cancer research has come of age.

Investigations of malignancy began at the close of the 19th century with the study of animal tumors and transplantability of these tumors into new hosts. But only in the past 10 to 15 years has there been an acceleration in tempo and a surge of activity. As a result, the resources presently available have produced a pattern that makes cancer research today a vigorous, comprehensive operation. Likewise, the products of this research are impressive in their immediate significance and exciting in their implication of advances yet to be achieved.

SCOPE OF RESEARCH

One of the elements contributing to the pattern of cancer research has been the widening

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scope of investigations by an increasing number of scientists working on programs that have become nationwide and even worldwide in scale. The philosophy at the National Cancer Institute is that any idea, wherever it originates, and any good scientist should be supported with funds.

The cancer chemotherapy program of cooperative research established by the United States Government to discover and evaluate compounds for the treatment of cancer illustrates this point. The program is directed by the Cancer Chemotherapy National Service Center, which is sponsored jointly by the National Cancer Institute, Veterans Administration, Food and Drug Administration, and the Atomic Energy Commission; and two non-Federal agencies, the American Cancer Society and the Damon Runyon Memorial Fund for Cancer Research. The Center is located at the National Cancer Institute. Figure 1 shows the organization of the cancer chemotherapy program.

In the program, the research of a network of hundreds of independent university and hospital investigators, research laboratories, and industrial firms is supported by funds from the Institute and assisted by technical services of the Center. The program embraces three major phases: the acquisition and initial screening for anticancer activity of many thousands of chemical compounds a year, further testing of promising compounds in larger animals and in the laboratory to develop safe doses for human trials, and evaluation in extensive clinical trials. This work is supported by contracts and grants from the Institute, which this year allocated $23 million, 30 per cent of its $75 million budget, for the activities of the Center.

Another illustration of the widening scope of cancer research is found in the research grants programs of the Federal Government and the voluntary organizations. The National Cancer Institute supports some 1500 research grants in all aspects of the cancer problem; the cause and nature of cancer, characteristics of tumor growth and behavior, diagnosis and treatment. Emphasis has recently been given to virus research and,
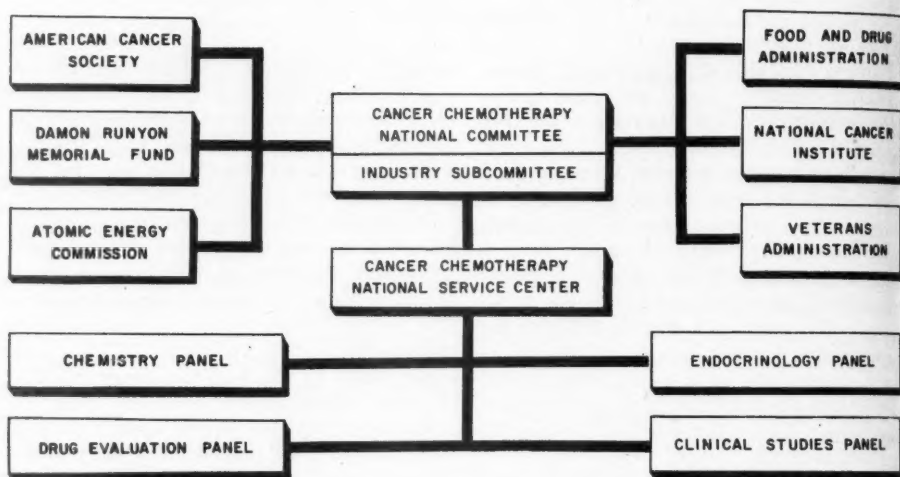
Cancer Chemotherapy Integrated Program

Fig. 1. The cancer chemotherapy integrated program is guided by the Cancer Chemotherapy National Committee. An Industry Subcommittee advises on industrial activity. The program is directed by the Cancer Chemotherapy National Service Center at the National Cancer Institute, Bethesda, Maryland.

as a consequence, this year the Institute is expanding the grants program in this area.

In recognition of the great need for training more young investigators, the Institute has organized also a program of research training grants, which provide predoctoral and postdoctoral fellowships for special research training and grants to qualified academic research centers to expand their research training programs primarily at the predoctoral, postdoctoral, and more advanced levels. The latter program extends and supplements but does not replace the research training opportunities available through research fellowships.

The Institute's investment in research grants is about $30 million this year, or 40 per cent of its budget. The American Cancer Society allocates 30 per cent of its yearly budget of some $30 million for support of cancer research. The Damon Runyon Fund allocates about $1 million a year similarly and several private foundations make available additional sums.

In efforts to stimulate increased international cancer research, the National Cancer Institute

supports research in other countries through awards of a limited number of grants to foreign scientists. It also supports foreign research fellowships and invites foreign scientists to the United States for research and study for varying periods of time. The mounting international character of cancer investigation is amply illustrated by the successful Seventh International Cancer Congress, which met in London in July 1958 and was attended by some 2500 members from 63 countries. Such meetings are sponsored every 4 years by the International Union against Cancer, which sponsors symposia, publishes an international cancer journal and organizes working committees to promote international agreement on cancer terminology. The International Union also serves as consultant on cancer research to the World Health Organization.

In recognition of the increasing need for a unified attack on disease, the Federal Government is moving into greater participation in international medical research activities through programs of the National Institutes of Health, of which the Cancer Institute is a constituent. A

grant of $300,000 was awarded recently by the National Institutes of Health to the World Health Organization to study medical research needs and resources around the world and to stimulate planning for international medical research. In addition, just a few weeks ago, Senators Lister Hill and Hubert H. Humphrey introduced a bill to appropriate $50 million a year for a National Institute for International Medical Research, which would be part of the National Institutes of Health. A similar bill was introduced in the House of Representatives by Congressman John E. Fogarty.

There has been an increase in activities in the translation and distribution of non-English research papers, particularly from the Russian literature. Russian scientific publications are now available in translations of journals, monographs, and individual papers.[1] Many of the translations are prepared as part of the National Institutes of Health Russian translation program; others are published with the aid of grants or contracts from the National Institutes of Health or the National Science Foundation. In addition, the National Institutes of Health publishes a monthly list of translations and provides a lending service.

FINANCIAL SUPPORT

Another element in the pattern of cancer research, financial support, is an obvious one. Nevertheless, the rate at which it has grown is somewhat extraordinary. The appropriation for the National Cancer Institute went up from $548,700 in 1946 to $14½ million in 1948. The American Cancer Society raised $850,000 by public subscription in 1944, but in 1945 these donations were increased more than 4-fold, to a total of $4 million. By 1948, contributions reached nearly $13¼ million. Since then, both agencies have continued to receive increasing support so that today the Society operates at a level of some $30 million, and the Institute at $75¼ million. The availability of such large sums shows clearly that the public is increasingly aware of the necessity for a scientific attack on the cancer problem and is willing to support this procedure.

COOPERATIVE EFFORT

The third element that I shall discuss in the pattern of cancer research, cooperative effort, owes its presence to the nature of cancer, which after more than half a century of research still remains an enigma. Again and again scientists have been frustrated in their efforts to solve the basic problems of cancer, as, for example, "What is early cancer?" The biologists, biochemists, geneticists, radiologists, epidemiologists, and, more recently, the virologists, immunologists, and serologists, have joined in the attack on cancer and have contributed tremendously to basic knowledge of cells, growth, and metabolism. Scientists are making deliberate attempts to become skilled in overlapping areas of research; for example, virologists trained in biochemistry and genetics, cytochemists, and radiobiologists are turning their efforts to cancer research. Perhaps as this trend continues a synthesis will result in which cancer research will no longer be considered the simultaneous activity of many interdependent sciences, but a scientific discipline in its own right, and the oncologist will make use of all the basic information and powerful techniques of the contributing sciences.

The organization of the clinical trials under the direction of the Cancer Chemotherapy National Service Center illustrates the application of the principle of cooperative effort which was undertaken to overcome some of the difficulty inherent in research with patients. Pooling of patient material makes possible the "telescoping of time" by bringing together in a comparatively short time quantitative data on sufficiently large numbers of different types of cancer, so that the results can be adequately and meaningfully interpreted.

There are 17 cooperative study groups of some 6 to 12 investigators each, representing over 175 hospital services throughout the United States, which have been formed to evaluate potential anticancer drugs in clinical trials. About 1 out of 1000 compounds reaches this stage. In a few groups, preliminary studies are in progress to evaluate the use of drugs as an adjunct to surgery.

Each study group is assisted by the Center in developing an experimental protocol, which includes the criteria for diagnosis, treatment schedule prescribed, measurements to be made, and criteria for response. The study groups analyze their results and publish them in the scientific literature. They also report their findings to the Center, which makes the information available to other investigators in the program.

About 70 materials are now undergoing clinical trials in some 3000 patients. Some of the materials

are those already in use and are being tested to obtain data under the controlled conditions of the clinical trials. Others are recently developed compounds, including 5-fluorouracil, developed by Heidelberger and associates[22] at the University of Wisconsin, and 3',5'-dichloroamethopterin, developed by the Lederle Laboratories, Pearl River, New York, and tested in the laboratory by Goldin and associates[16] at the National Cancer Institute.

Early studies of these compounds have been reported and they make an appropriate point of departure for a brief review illustrating some of the products of cancer research in various areas.

RESEARCH ON NEW DRUGS

5-Fluorouracil is a member of a new class of tumor inhibitory compounds, 5-fluoro pyrimidines. These are pyrimidine antagonists, or antimetabolites, which are believed to accomplish their anticancer action by blocking an essential sequence of events involved in the biosynthesis of nucleic acid. In the Ehrlich ascites carcinoma of mice, 5-fluorouracil produced a 420 per cent increase in survival time. Several animals survived 100 days, at which time they were tumor free, as judged by gross examination and attempted transplantation experiments.[22] When the drug

was given in adequate dosage to 35 patients afflicted with far advanced cancer, 9 (25 per cent) showed objective regression of solid tumors. Among the types of cancer that responded to the drug were tumors of the breast, liver, rectum and other sites. The majority of the patients reported subjective improvement and decrease of pain to such an extent that analgesics were no longer required. The drug produced marked toxic reactions, which were of relatively short duration once the drug was withdrawn. Additional related compounds are being studied to develop drugs that are less toxic.[2]

3',5'-Dichloroamethopterin is related chemically to methotrexate, a folic acid antagonist that is used in the palliative treatment of human leukemia. When tested by a drug assay procedure developed by Goldin and associates,[17] Methotrexate was the most effective of a group of 38 compounds, including reserpine, 6-mercaptopurine, thioguanine, and 8-azaguanine, in producing increased survival of mice with advanced systemic leukemia L-1210. Control animals inoculated with this leukemia succumbed in about 10 days, whereas those receiving Methotrexate had a median survival time of about 30 days, when treated daily from day 7. As shown in figure 2, under similar conditions, mice receiving 3',5'-di-
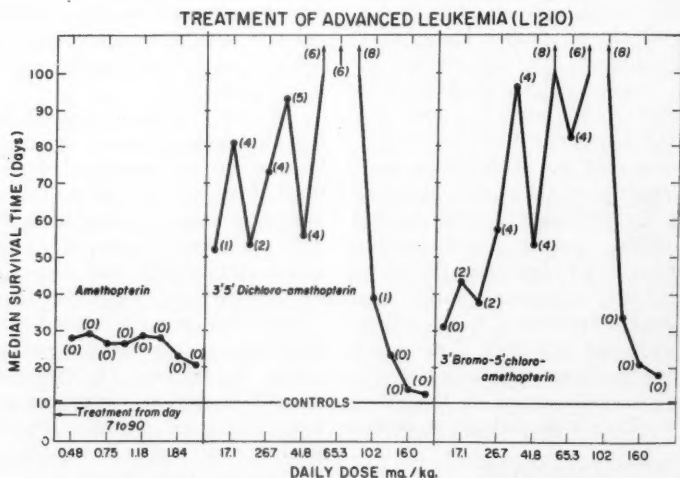

FIG. 2. Treatment of advanced mouse leukemia (L-1210) with Methotrexate (amethopterin) and two of its dihalogenated derivatives. The median survival time obtained, employing 10 mice, is shown at each level of daily treatment for each agent. Median survival times in excess of 100 days are indicated by arrows pointing upward. Figures in parentheses are the numbers of 100-day survivors in the various experimental groups.

chloroamethopterin and another derivative, 3'-bromo-5'-chloroamethopterin, had a median survival time of more than 100 days.[18]

In one experiment, on day 100, 41 survivors remained out of 130 mice treated at various dosage levels of the dichloro compound and 42 remained out of another group of 130 mice treated with the bromochloro compound. Some of the animals were still alive and healthy at the end of 6 months. Although these results obviously do not guarantee similar results in clinical studies, they provide an experimental demonstration of the feasibility of controlling systemic leukemia by drugs and show that advanced mouse leukemia is a good model system for systematic studies of compounds developed by altering the structure of known drugs.

DETECTION BY THE CYTOLOGIC TECHNIQUE

A project established a few years ago in the Memphis area by the National Cancer Institute with the cooperation of the University of Tennessee and other local medical and health groups showed the usefulness of the cytologic technique as a case finding procedure for the detection of early uterine cancer in large populations. An additional analysis by Dunn and associates[7] of the data obtained in the screening of 83,000 women in the Memphis project has shown that invasive uterine cervical cancer may be asymptomatic for 2 to 3 years after onset. Uterine cervical cancer can be detected during this symptom free period by cytologic examination of vaginal fluid.

In related research, Pruitt and associates[26] have reported progress in studies of an instrument
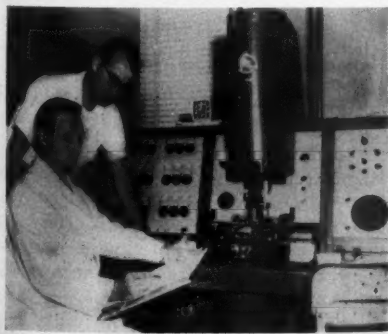
Fig. 3. Cytoanalyzer, an electronic instrument under development to speed the examination of specimens obtained in the cytologic test for uterine cancer.

that is being developed to speed the examination of specimens obtained in the cytologic test for uterine cervical cancer. Figure 3 shows the cytoanalyzer, which is an electronic instrument consisting of a scanning microscope, computer and analyzer. Glass slides with specimens of vaginal fluid containing exfoliated cells are placed in the cytoanalyzer, which produces information on the number of cells present in the specimen and the size of their nuclei. On the basis of this information, an investigator classifies the specimen as negative, or as suspicious or positive and therefore to be retained for further examination.

In a study of 1095 slides examined in the cytoanalyzer, 1075 were known to be negative and 20 were known to be positive or suspicious. The machine gave accurate results for all the positive or suspicious slides and 40 per cent of the negative slides. The cytoanalyzer was about twice as accurate in examining slides from premenopausal women as from postmenopausal women. This difference is explained by the fact that nonmalignant cells with large nuclei often appear in clusters in the vaginal fluid of postmenopausal women. The successful results obtained in the study were attributed largely to an improved method of preparing the cells in a monolayer on the slides.

IDENTIFICATION OF MALIGNANT CELLS IN BLOOD

Much effort is being made to determine accurately the frequency of malignant cells in the circulating peripheral blood and the significance of the presence of such cells. Excellent contributions to this effort have been made in the past few years by Engell[11] and by Sandberg and Moore.[25, 28, 29]

Malmgren and others[24] at the National Cancer Institute have now reported the development of a quantitative technique for preparing human whole blood so that it can be examined cytologically. Preparation of the blood for microscopic examination involves the processing of 20-ml. samples by a combination of filtration, centrifugation, and addition of the enzyme, streptolysin O, which removes erythrocytes and certain white blood cells without altering or removing tumor cells. The residual material is collected on several millipore filters, each of which is stained, mounted and examined. This process requires approximately 2 hours from the time the blood is collected until it is ready for examination. Approxi-
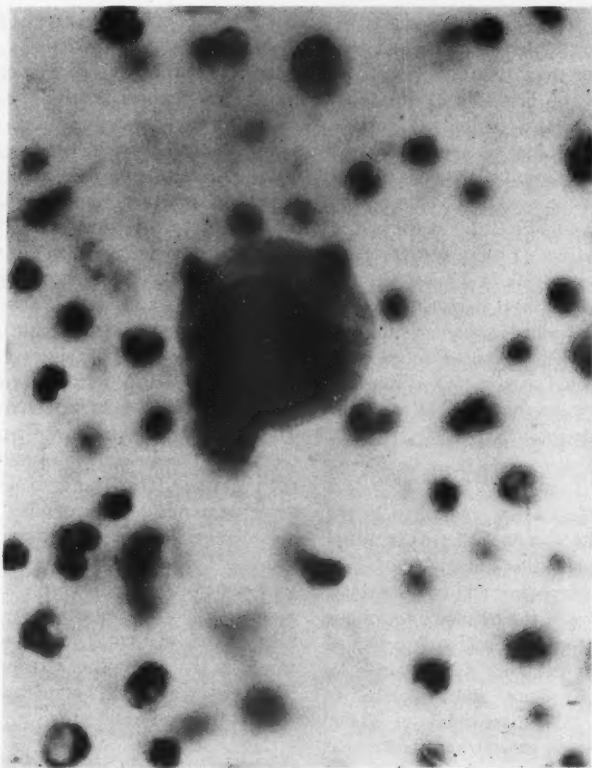
FIG. 4. Malignant cell found in peripheral blood of a patient with carcinoma of the kidney (× 1380) (From Pruitt, J. C., Hillberg, A. W., and Kaiser, R. F.: Malignant cells in peripheral blood. New England J. Med., *259:* 1162, 1958.)

mately 20 minutes is required for screening each slide. In tests of the technique on samples of whole blood to which had been added a known number of tumor cells obtained from a variety of sources, the margin of error was less than 10 per cent and the tumor cells remained morphologically intact.

Use of the technique for the examination of peripheral blood obtained from a vein in the antecubital fossa of 100 patients with a diagnosis of cancer and 200 presumably well people with no evidence of cancer and no history of the disease revealed that cytologically malignant cells were identified in 39 per cent of the cancer patients and suspicious cells were present in an additional 12 per cent.[27] In the control group, on the other hand, cells that were considered to be cytologically malignant were found in 1 person, or 0.5 per cent. Figure 4 shows a malignant cell found in the peripheral blood of a patient with carcinoma of the kidney.

As shown in table 1, the relation of type of lesion to the presence or absence of malignant cells was not clear cut. Malignant squamous cells appeared to exfoliate into the blood at least as often as cells from adenocarcinomas. Sarcomas exfoliated cells into the blood with about the same regularity as carcinomas. It will be interesting to follow the studies of peripheral blood to learn whether manipulation of a tumor at the time of operation actually may cause a spraying of malignant cells into the blood stream and whether patients with cancer cells in the blood and no evidence of metastases develop further lesions.

USE OF ILEUM AS SUBSTITUTE BLADDER

The problem of the management of patients whose normal urinary flow has been disrupted as a result of disease or operative procedure or both has been studied by Jude and Pieper,[23] who have

TABLE 1
*Type of malignancy**

Lesion	Total Cases	Posi- tive Cases	Suspi- cious Cases	Nega- tive Cases
Carcinoma.............	87	31	11	45
Adenocarcinoma....	66	21	7	38
Squamous cell......	21	10	4	7
Sarcoma..............	4	2	1	1
Lymphoma...........	2	2	0	0
Other:				
Malignant mesothe-				
lioma.............	1	1	0	0
Astrocytoma........	2	1	0	1
Malignant thy-				
moma............	1	0	0	1
Melanoma..........	3	2	0	1

* Reproduced from paper by PRUITT, J. C., HILBERG, A. W., AND KAISER, R. F.: Malignant cells in peripheral blood. New England J. Med., *259:* 1163, 1958.

reported the development of a surgical technique making use of ileum as a substitute bladder. In a number of female, mongrel dogs subjected to a procedure in which a bladder was constructed from a 6- to 12-cm. segment of terminal ileum, urinary flow was diverted through the isolated bladder and the nonfunctioning, autogenous bladder was left intact. Studies of urine and blood chemistry carried out serially after the operation showed no complications directly related to the operative procedure. These successful results have suggested clinical application of the technique in patients subjected to pelvic exenteration.

VIRUSES AS A CAUSE OF CANCER

For more than 50 years, evidence that viruses cause cancer in animals has been accumulating, with the result that interest in the possible viral etiology of human cancer has increased steadily. Beginning in 1908 with the work of Ellermann and Bang on the transmission of fowl leukemia by means of cell free preparations, the scientific literature records the discovery, in 1911, of the Rous sarcoma virus of chickens; 1933, the Shope papilloma virus of rabbits; 1934, Lucke's virus of the leopard frog; 1936, Bittner's mammary tumor agent of mice; 1951, Gross' mouse leukemia agent, which may involve one or more viruses.[30]

FIG. 5. Swiss mouse with small bilateral salivary gland tumors, multiple mammary tumors, thymic tumor, and hair follicle tumors.

In the last couple of years, two more viruses have been reported. Stewart and associates[31] observed the development of multiple tumors in newborn mice inoculated with cell free extracts of parotid gland tumors or leukemic tissue that had been carried in tissue culture. All mice that developed such tumors had primary parotid gland tumors; some also developed tumors of the thymus, adrenals glands, and mammary glands. Figure 5 illustrates the results observed in mice.

As shown in figure 6, tumors were induced also in hamsters by the agent present in tissue cultures containing minces or extracts of mouse leukemias.[8] The tumors, which were sarcomas and vascular tumors almost exclusively, occurred at an age when extremely few spontaneous neoplasms had been described in hamsters.

Figure 7 shows that renal sarcomas and subcutaneous tumors were produced in rats by the same agent.[9] The response of rats to the agent was somewhat less striking than in mice and hamsters.

Further investigation showed that the mouse tumor agent has biologic and physical properties of a virus.[10] Now known as the polyoma virus, the agent is rather remarkable in that it crosses strain and species barriers in producing tumors. In addition, its tumor producing activity is in-
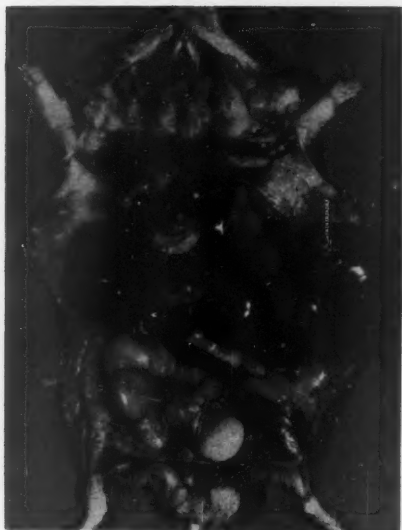
FIG. 6. Hamster with mediastinal tumor involving the heart and large vessels, hemangiomas and sarcoma of liver, and two subcutaneous tumors.
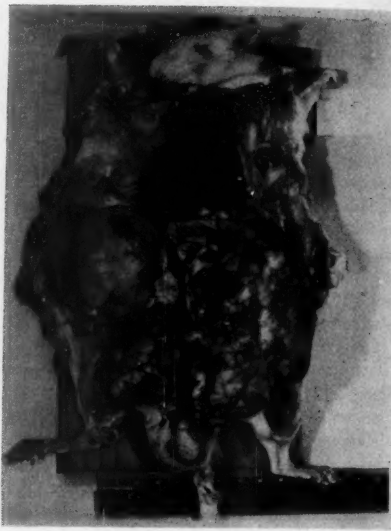

FIG. 7. Rat with renal sarcoma in the kidney and extension of the tumor to peritoneal surfaces of abdominal viscera.

creased by alternate passage through tissue culture and mice or hamsters. Its property of producing neutralizing antibodies in rabbits was utilized in a "neutral mixture" of polyoma virus and antibodies, which prevented production of tumors in hamsters by the virus.[32]

Friend[12] reported the discovery of a filterable agent that induced a leukemialike disease in mice of any age within as short a period as 2 or 3 weeks after inoculation. This agent was found during the course of studies on the effect of cell free preparations of the Ehrlich ascites tumor in infant Swiss mice. Friend[13] also developed a formalin killed vaccine that protects the mice from developing the disease when they are challenged with live virus.

By the latest techniques of electron microscopy, viruslike particles have been visualized directly in tumor tissues of mice and chickens.[3, 21] Dmochowski and Grey[5] reported also evidence of viruslike particles in biopsy material from an enlarged cervical lymph node of a patient with acute lymphatic leukemia. The cellular changes were similar to those evident in mouse leukemia.

Much new information has been obtained in recent years about the nature and characteristics of viruses and the chemical constitution and metabolism of cells. As a result, new ideas are emerging to suggest how cancer viruses may attack normal cells. Interest centers about a key substance, nucleic acid, which is a complex molecule present in all cells and possesses the property of replication. Nucleic acid is localized in the chromosomes and is generally believed to be the active material of the gene, transmitting coded information from an organism to its offspring during reproduction.

Nucleic acid is an important component of viruses and, according to very recent evidence, capable of initiating an infectious process. Viruses are so remarkably similar to genes that they are sometimes called "naked genes" or "infectious genes."[30] Furthermore, recent studies with bacteria and bacterial viruses have implicated viruses even more deeply in the genetic processes of the host. By a process known as transduction, genetic material, and thereby hereditary traits, can be transferred by a virus from cell to cell. This important discovery was made by Zinder and Lederberg,[34] who found that a bacterial virus carried the bacteria's own genes from one cell to another, infecting one bacterium with hereditary material from another.

The thought is, then, that a viral nucleic acid might enter a host cell and be incorporated into

the genetic structure of the cell. In this form it might be nonpathogenic and noninfectious in the usual sense, but would multiply at least once with each cell division, and thus be regarded as infectious in the sense that genes or chromosomes are infectious.

Such a viral nucleic acid would be subject to shock or to chemical or physical stimulants, such as x-rays, ultraviolet light, nitrogen mustard; in other words, carcinogenic agents, which could cause it to mature, greatly increase its rate of replication and thus enable it to act as an independent functional unit. The result would be production of a mutant, perhaps cancerous, cell.[30] Such studies are approaching the boundaries of life itself and the results make a fascinating story.

IN CONCLUSION

Cancer research is organized and supported in a manner that was considered only remotely possible by the most visionary investigators a few years ago. The available funds have been increased tremendously, many scientific skills enlisted, techniques and instruments refined, and basic knowledge of cells and growth expanded, with the result that a concerted effort is now possible.

The problem is more clearly defined than ever before. Cancer continues to be the second leading cause of death in the United States; second only to the cardiovascular diseases. An estimated 450,000 new cases are diagnosed every year. Deaths total about 250,000 a year, and there are some 700,000 cases under treatment at any given time.

A sharp rise observed in lung cancer in recent years has spurred intensive study of the etiology of this form of cancer. Epidemiologic and laboratory studies to date implicate heavy cigarette smoking[6, 33] and the pollution of air by carcinogenic substances[4, 14] as factors operative in the increased incidence of lung cancer. The trend in leukemia as shown by analysis of recorded mortality is still upward, but the rate of increase in the past 10 years has not been as great as in previous years.[15]

On the other side of the ledger, a steady decline has been observed in the incidence of stomach cancer in the United States during the past several decades.[20] Suggested avenues for further study to clarify the nature of this trend include the role of endogenous factors and the influence of diet. Also, progressive improvement has been noted in the 5-year survival rate in cancer of the uterine cervix, due partly to education and earlier diagnosis, partly to more expert treatment, and partly to a rising level of medical care.[19] Twenty years ago, 1 in 4 cancer patients survived 5 years after diagnosis of his disease. Today, the proportion is 1 in 3 patients, or 150,000 persons a year.

The task before all of us is to detect early cancer and to treat it promptly and adequately; to recognize carcinogenic hazards and to prevent them; and, finally, to educate and inform the medical profession and the general public of the progressive advances in knowledge of cancer. These are our missions and our goals.

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National Institutes of Health
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BYPASS GRAFTS IN SMALL ARTERIES: AN EXPERIMENTAL COMPARISON OF FREEZE-DRIED ARTERIAL HOMOGRAFTS, AUTOGENOUS VEIN, AND CRIMPED DACRON*

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The evolution of arterial surgery, from the standpoint of both materials and methods, has been frequently and adequately recorded. It is a continuing story. There is now a relative unanimity of opinion as regards the replacement or bypassing of major arteries. Synthetic grafts are unchallenged as the ultimate answer. A considerable difference of opinion remains, however, as to the ideal graft for the smaller peripheral arteries.[2, 7-9]

Although the incidence of aneurysmal dilation of autogenous vein grafts when used in the surgery of major arteries has been found impractically high,[7] this has not proved to be true in the extremities.[2, 7-9] The late degenerative changes in arterial homografts, in spite of initial success, is well documented.[10] As yet, there is no conclusive evidence that the proper fabrication of a prosthetic has been achieved to the extent that the success with autogenous vein as a peripheral arterial graft can be matched.

This experimental study was initiated with the hope that a standard procedure would result in a control series of autogenous vein grafts in small arteries adequate to serve as a basis for comparison with arterial homographs and in particular the various synthetic grafts. Segments of occluded femoral artery of uniform length were bypassed in mongrel dogs with autogenous saphenous vein, crimped Dacron, or freeze-dried arterial homografts. Long term studies will be required to assess the final results, but the incidence of early failures is of obvious importance in the avoidance of futile efforts with unsuitable materials. All of the experiments reported in this communication constitute an early evaluation of the grafts used (less than 1 year).

MATERIAL AND METHODS

Studies were carried out in 20 adult mongrel dogs chosen at random except for size (20 kg. or more). The anesthetic agent was veterinary Nembutal. Both inguinal regions and thighs were shaved and prepared with soap, ether and tincture of Zephiran. An additional area over the saphenous vein was prepared in the same manner, (right rear extremity).

A segment of saphenous vein adequate for the purpose was dissected free, branches ligated with 4-0 silk, and the segment removed and placed in saline. Simultaneously, either a freeze-dried arterial homograft was reconstituted or a crimped Dacron graft (5 mm.) sterilized. The femoral artery was exposed bilaterally through oblique incisions.

The length of femoral artery available for bypassing was limited since it was decided to leave the inguinal ligament undisturbed. Accordingly, a 1-inch segment of femoral artery was occluded between ligatures (fig. 1, *1* and *4*) and the occluded segment partially divided in order to prevent recanalization, (Fig. 1, *1, arrow*).

End-to-side bypass grafts were then performed about the occluded segments. Reversed autogenous vein was routinely employed on the left; either arterial homograft or crimped Dacron, on the right. The average diameter of the bypassed segment was 3.5 mm. The technique used throughout is illustrated in figure 1. Everting mattress sutures of 5-0 or 6-0 arterial silk were placed at either angle but continued as a whipstitch with small bites and with care to prevent inversion (fig. 1, *2* and *3*). The homografts and the crimped Dacron grafts were simply beveled, as illustrated (fig. 1). The vein grafts were slit longitudinally on their anastomotic surface and the corners trimmed. The anastomotic stoma was estimated at 2 to 3 times the lumen of the femoral artery.
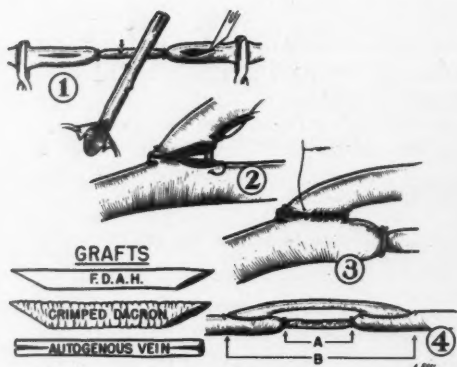
Fig. 1. Experimental bypass grafting of small arteries (see text for details).
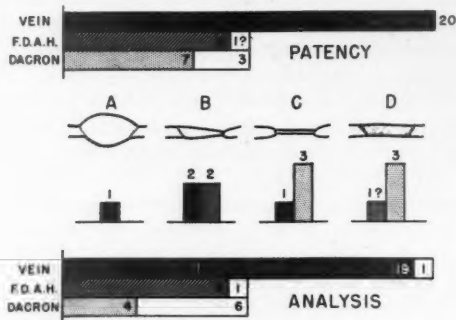

Fig. 2. Results: *A*, dilation of graft; *B*, slight distal narrowing; *C*, marked narrowing; *D*, occluded graft (see text for details).

The over-all length of the bypass grafts was approximately 5 cm. (fig. 1, *4B*). No heparin was utilized during the procedure. Antibiotics were given postoperatively on only one occasion because of a prior infection in the operative area.

Arteriograms (50 per cent Hypaque), performed in a retrograde manner through a carotid artery, were obtained in the majority of experiments at the time of final evaluation (figs. 3 to 5). In the remainder there was no question of patency of both grafts, by virtue of bounding pulsations. Four of the animals operated upon early in the study were killed. Microscopic examination of the specimens revealed nothing inconsistent with previous studies.

RESULTS

The time interval between the original operative procedure and the final evaluation reported

Fig. 3. Arteriogram showing patent arterial homograft and autogenous vein grade (*left*).

herein ranges from 1 to 8 months. The animals served as their own controls since grafts of different types were placed in each. All of the vein grafts were patent (fig. 2). One of the two autogenous vein grafts other than saphenous (this one jugular; the other, femoral) was dilated as indicated (fig. 2, *A*). In addition, there was slight but noticeable distal narrowing of two other vein grafts (fig. 2, *B*). Rather marked narrowing was present in one (fig. 2, *C*); in the protocol of that experiment it was noted that the graft was "under too much tension."

Of 10 freeze-dried arterial homografts, all were patent except questionably 1 (fig. 2, *D*). The latter animal developed a large hematoma in the operative area on that side in the early postoperative period. An extremely small lumen was present and probably represented recanalization. In addition, slight distal narrowing was present in two of the homografts (fig. 2, *B*).

Of the 10 crimped Dacron grafts (all preclotted in the wound) 3 were found to be occluded (fig. 2, *D*) and 3 markedly narrowed (fig. 2, *C*).

As a final analysis (fig. 2) it was found that 19 of 20 vein grafts were entirely satisfactory (patency, 100 per cent); 9 of 10 arterial homo-

FIG. 4. Arteriogram showing patent vein graft (*left*) and occluded Dacron graft
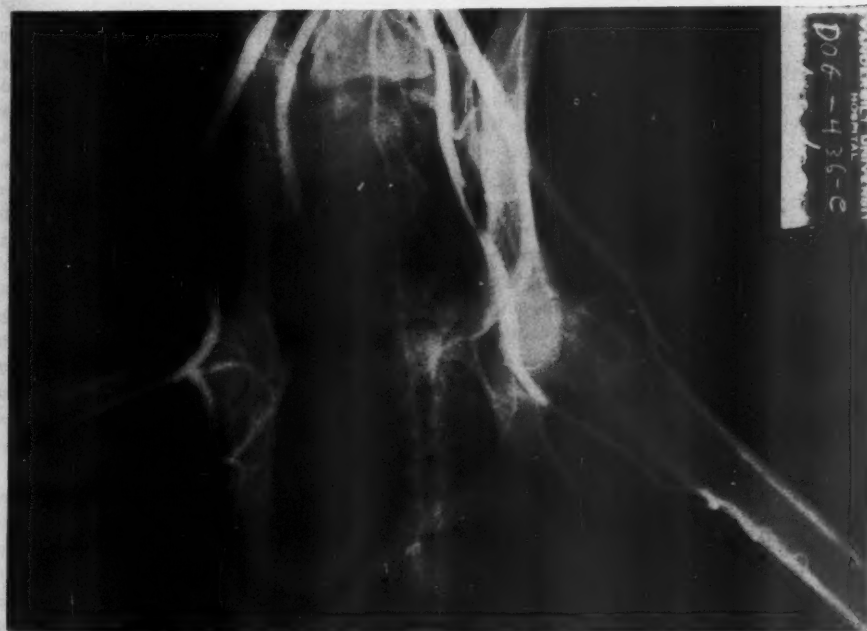

FIG. 5. Arteriogram showing patent vein graft (*left*) and Dacron graft

grafts, satisfactory (patency, 90 per cent); and only 4 of 10 crimped Dacron grafts in that category (40 per cent) (patency, 60 per cent). Illustrative arteriograms demonstrate a patent homograft and vein graft (fig. 3), a patent vein graft and an occluded Dacron graft (fig. 4), and a patent vein graft and Dacron graft (fig. 5). The sites of the grafts are not easily identifiable in either figures 3 or 5.

DISCUSSION

The early (1 to 8 months) follow-up studies, in this group of experimental small arterial grafts in dogs, indicate an obvious superiority of autogenous vein and freeze-dried arterial homografts over crimped Dacron. There is no significant difference between the vein and the arterial grafts. The certainty of late degenerative changes in the homografts[10] as demonstrated by numerous investigators leaves autogenous vein as the graft of choice among those studied. The lack of aneurysmal dilation of these grafts in small vessels is apparently related to adequate surrounding tissue support as opposed to vein grafts in the central arteries.[2, 7-9] Excellent comparative studies of various synthetic grafts have been reported by Harrison[6] and Edwards and associates.[1, 3-5] Numerous factors influencing the efficacy of these materials are referred to. All seem to be directly correlated with the wettability of the fiber.[3, 6] Of all studied, Teflon seems by far the best performer.[3, 6] It does not absorb water and does not lose tensile strength in long term studies. There remains, however, the very real question of fabrication. We were impressed with the routine induration about the Dacron grafts utilized in this study in the early postoperative period. Dacron has been shown, apparently by by virtue of its "wettability," to cause more tissue reaction than Teflon. It was our feeling, however, that excessive seepage of blood through the interstices of the knitted grafts during the period of reaction from the anesthestic accounted in large part for the surrounding induration in the early postoperative period. We were impressed, conversely, by the lack of reaction about either the autogenous vein grafts or the freeze-dried homografts. We are, therefore, inclined to feel that the porosity of the Dacron grafts accounted for the poor early results noted.

The standardization of the experimental procedure utilized along with the 100 per cent patency of the autogenous vein grafts leads us to feel that we have a good basis for comparison with the synthetic grafts.

Comparative studies of knitted and woven Teflon grafts in the same animal with the standard technique described are underway. Although the technical difficulties with the woven graft are somewhat greater than with the knitted, they are certainly no greater than with the utilization of an extremely thin walled saphenous vein in the dog.

If none of the available synthetics proves as satisfactory as autogenous vein, another practical question arises. Can long segments of the saphenous vein be gently stripped with an extraluminal stripper, halting at each communicating vein to avoid excess trauma, with a resulting autogenous vein graft of sufficient length to perform a successful femoropopliteal bypass? The time required for the direct exposure and dissection of the desired length of autogenous vein is, in some respects, impractical.

If a stripping procedure, gently performed, can be done with an adequately low incidence of subsequent thrombosis, one answer is available to the problem of small arterial grafts. Thromboendarterectomy for arterial occlusive disease involving short segments is not under consideration here. It would seem advisable, in any event, to continue the search for the properly fabricated synthetic graft for use in the surgery of small arteries.

SUMMARY

An experimental comparison in dogs, of grafts bypassing a segment of femoral artery, has been presented. Autogenous vein, freeze-dried arterial homografts, and crimped Dacron were utilized. The results are reported at from 1 to 8 months. Within the time limits of the study there was little to choose between autogenous veins and arterial homografts. The crimped Dacron grafts proved to be unsatisfactory for use in vessels of this size.

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Editorial
PATIENT'S COMFORT

The value of prolonged intranasal gastric intubation following certain surgical procedures has been well established. Likewise, the discomfort associated with this valuable procedure is long remembered by the patient. The discomfort of prolonged nasogastric suction invariably lingers in the minds of our patients today, not unlike the disagreeable memories of ether induction anesthesia in the good old days. Is this discomfort any longer necessary? Those who have used gastrostomy when prolonged postoperative decompression is indicated tend to be convinced by their own observations and the testimonials of their patients that patient comfort is greatly enhanced by this procedure.[1]

Surgeons have always been cautious in their use of gastrostomy. They retain unfavorable impressions of this procedure when it has been utilized for feeding purposes in cases of inoperable malignancy proximal to the stomach. Their inherent fear of creating a persistent gastric fistula or producing late symptoms from fixation of the gastric wall to the peritoneum combined with the danger of leakage and peritonitis are common objections to this procedure. Frankly, nasal suction is so common that little sincere sympathy for the patient is ever considered unless the intubation is required for many days.

Aside from patient comfort, there are numerous instances in which nasal suction should be preferably avoided following abdominal surgery, for example: the elderly uncooperative patient; the presence of obstruction to the nasal passages; pulmonary disease associated with a productive cough; or the chronically ill patient with few if any remaining veins for intravenous therapy. In such cases the gastrostomy tube is a useful and efficient route after several days for the maintenance of fluid, electrolyte and caloric requirements.

Certain technical points have proved useful in the performance of gastrostomy. Any point in the anterior gastric wall which can be easily attached to the overlying peritoneum of the anterior abdominal wall should be selected. Either a mushroom catheter, size no. 16, or a Foley catheter is introduced 7 to 10 cm. into the stomach through a small stab wound. Bleeding in the gastric wall is controlled by the two or three silk sutures taken to constrict the gastric wall about the catheter. A liberal purse-string suture is then inserted and tied to make certain that the gastric wall about the catheter is inverted into the lumen of the stomach. Inversion of gastric wall about the catheter provides assurance against the possibility of a gastric fistula. A stab wound is made in the left epigastrium in the area previously tested for easy apposition of the stomach to the peritoneum and 5 cm. or more from the peritoneal margin to avoid possible contamination of the peritoneal closure. Ordinarily four to six silk sutures are taken in the peritoneum around the catheter and in the opposing gastric wall. A sufficient number is taken to seal the area about the tube so that accidental early removal of the gastrostomy tube would not result in peritoneal contamination.

The catheter is anchored to the skin with one silk suture supplemented by an adhesive dressing separated from the major wound. The majority of gastrostomy tubes are removed in 7 to 10 days. Prompt closure will follow.

The indications for this procedure, in our experience, most commonly arise following relief of intestinal obstruction, colon resections, vagotomy combined with either a short circuiting procedure or a 50 per cent gastric resection and, finally, a miscellaneous group of major abdominal procedures in debilitated patients in whom the need for prolonged fluid and caloric supplementary feeding can be anticipated.

The gastrostomy tube has permitted repeated studies on gastric acidity while under fasting conditions, as well as in response to the ingestion of a variety of foods and medications. The short term "Beaumont experimental preparation" may well provide valuable assistance in furthering our knowledge of gastric response in the early postoperative period. Long practiced routines are not easily broken. Consider your own reaction to prolonged nasogastric suction before closing the peritoneum of the next patient that you know will surely need the benefits of prolonged gastric decompression.

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Book Reviews

Lectures on Epilepsy. Edited by A. M. LORENTZ DE HAAS. Published under the auspices of the Netherlands Society of Psychiatry and Neurology. 700 pp., Elsevier Publishing Co., Amsterdam, 1958.

This book is based on writings of various workers in the field of epilepsy connected with both institutionalized and noninstitutionalized patients. It amplifies the work being done in European countries, notably France, regarding the personality factors in these patients. Little on this subject has been written in this country. These types of cases form the minority of epileptics.

The first article, by M. David and M. B. Dell of Paris, discusses temporal lobe epilepsy and its surgical treatment. They divide this type of epilepsy into two groups, one with purely a focal component and the second with more widespread or multiple areas of origin, but both with similar EEG findings. Bilateral temporal foci were considered poor surgical risks. They propose that surgery be done in the first type only, with a minimum of tissue being removed, suggesting only the excision of the anterior part of the hippocampus, the uncus and the amygdaloid nucleus. Their results compare favorably with results of those who do a more extensive excision.

The next three chapters deal with psychic disturbances in epileptics. H. Vislie and G. F. Henriksen of Norway evaluated 162 patients with epilepsy seen in the Diagnostic Station for Epilepsy, University Hospital of Oslo. They divided them into three groups: (1) progressive organic dementia, (2) probable organic dementia, (3) no dementia. In 40 per cent of the cases some minor neurologic findings were present in addition to the seizures. They were all classified according to relation of psychic symptoms to onset of seizures; social adjustment; I.Q.; characteristics of seizures as to time, age, duration and type; EEG findings; extent of brain lesion.

In Chapter 3 H. Landolt of Zurich, Switzerland, discusses the serial electroencephalographic findings during psychotic and schizophrenic episodes. He felt that four types of psychotic episodes were distinguishable by the EEG: (1) postparoxysmal twilight states (a general decrease in consciousness) with the EEG finding of a diffuse delta-theta dysrhythmia bilaterally; (2) the petit mal status with continuous spike-and-wave findings in the EEG; (3) productive psychotic episodes with "forced normalization" in the EEG or "epileptic mania" (these patients, during mentally normal periods, have seizures and abnormal EEG's); (4) psycho-organic episodes such as induced by overdosage of anti-epileptics, or organic pathology such as tumor, infection, and atrophy with the EEG showing more abnormality.

EEG's were also done in a group of noncatatonic forms of schizophrenic patients. Conclusions were drawn that in treatment of these patients the EEG should be used as a guide, and what they call a "normally" pathologic EEG should be aimed at since these patients during their most involved periods have a normal EEG but during periods of remission have an abnormal EEG.

In Chapter 4 A. M. Lorentz de Haas and O. Magnus of Heemstede, The Netherlands, discuss the electroencephalographic findings in patients with episodic mental disorders and, as in the previous chapter, the twilight states showing the spike-slow wave complexes considered to be due to centrencephalic epilepsy. They point out the lack of aggression of patients in this state during their seizures. The second group they discuss are the dysphoric states in which most of the patients showed aggression associated with their seizures, all showing very abnormal EEG's of all types. The last group of psychotic states is divided into paranoid, depressive and psychotic states of uncertain nature, all with seizures. In summary, they feel that both the psychotic predisposition and the pathologic symptoms of the epilepsy contributed to the total picture in these psychotic patients.

RUTH W. BALDWIN, M.D.

Cardiac Arrest and Resuscitation. By HUGH E. STEPHENSON, JR., M.D. C. V. Mosby Company, St. Louis, 1958.

This scholarly text constitutes a much needed source of detailed material in the vital area of cardiac arrest. Both by virtue of his own personal experiences in clinical and experimental cardiac arrest, and also by the development and the maintenance of the Cardiac Arrest Registry at the University of Missouri School of Medicine, Dr. Stephenson has established himself as a foremost authority in the problems of cardiac resuscitation. The book he has written is not a simple manual, but rather a detailed reference type of book which does, however, contain many impor-

tant practical points. He has a number of distinguished collaborators who have added a great deal to the volume, from the standpoint of interesting reading and of important information. The style of writing is essentially scholarly rather than a down-to-earth rapid-fire flow of material. There is a tendency to dwell at some length at times on subject material (*e.g.*, section dealing with anesthesia and the etiology of cardiac arrest) which is not necessarily relevant to the problem of cardiac arrest itself. Also there is a good deal of quotation from various individuals who have worked in this area; this tends to increase the bulk of the volume but does not necessarily contribute to the ease of flow or comprehension in reading.

These criticisms are technical in nature only with regard to the style of writing. They do not detract from the tremendous contribution, singular among which is that this book will prove to be the important source of information governing all phases of the problem in cardiac arrest. The zenith of information becomes realized with Chapter 5, which deals with management of cardiac arrest. In this chapter the recommended procedures are outlined in detail very lucidly. Of especial interest is a list of four conditions in which the pericardium should be opened for resuscitation of cardiac arrest: for electrical defibrillation to allow direct applications of the electrodes to the myocardium, to permit a diagnosis of ventricular fibrillation when it is suspected but not definitely seen with the intact pericardium, in young infants, and in rupture of the heart during massage. A fifth indication might be included dealing with stab wound of the heart in which cardiac tamponade has occurred with blood filling the pericardial sac, resulting in inadequate massage. Of particular note in this chapter is a discussion of a hospital plan of action for cardiac arrest, in which a mobile cardiac resuscitation unit is described and recommended for usage. In this chapter a list of fallacies regarding cardiac arrest and resuscitation have been compounded and should be consulted by everyone interested in resuscitation of an arrested heart. The need for immediate action in instances of cardiac arrest is stressed along with the precaution of ascertaining the period of time in which the circulation has been ineffective. The author points out that the heart can usually be resuscitated but frequently neurologic damage has already occurred. Of particular importance is the section, by an attorney, dealing with the medical-legal aspects. Since there is a great deal of question about pursuing resuscitation with varying degrees of enthusiasm, depending upon the estimated time of loss of effectiveness of the

circulation, this particular section contains much valuable information and should be read with particular attention by everyone who may have occasion for being responsible for the management of cardiac arrest.

The" Prevention of Cardiac Arrest" is a particularly apt chapter and contains a useful body of information including stress upon the vago-vagal reflex as an important mechanism in the etiology of cardiac arrest. Numerous sources of conflicting material are quoted but in general the impression is gained that procaine is not very effective in preventing cardiac arrest.

The various techniques for elective cardiac arrest are discussed and it is concluded that the Melrose technique is the preferable one. The various cardiac arrhythmias and degrees of block, frequently observed after resuscitation, are dealt with by a prominent authority. Of unusual importance is the discussion of long term neurologic sequelae following cardiac resuscitation. Hypothermia is recommended to prevent these serious neurologic sequelae.

All in all this book serves as an excellent source of reference material because of (1) the scholarly presentation, (2) detailed material together with the various opinions offered by numerous workers in this area and (3) the extensive bibliography. Many practical points are also presented in a useful chronologic fashion. The text thus serves a dual purpose of being an encyclopedic source of information and a manual of practical management of cardiac arrest.

EMIL BLAIR, M.D.

Technique of Fluid Balance. By GEOFFREY H. TOVEY. 90 pp., Charles C Thomas, Springfield, Ill., 1957.

In the preface the author states his purpose in adding to the available literature another monograph on fluid and electrolyte therapy.

"Firstly I believe there is a need for a shorter account than most of those already published. Secondly I feel there is a growing tendency to make water and electrolyte therapy too dependent upon results of blood electrolyte estimations. One of the aims of this monograph therefore is to guide the doctor who has no laboratory, as well as those practicing in hospitals equipped with modern pathologic departments."

The work is short; the format is the usual one, beginning with descriptions of fluid spaces and normal electrolyte levels, rapidly going on to describe the more common alterations and their treatment and concluding with a brief description

of specific conditions and their treatment. Explanations of conditions, though of necessity brief, are fairly well illustrated by diagrams and outlines. The sections devoted to therapy are by practicality limited to maintenance and the more common alterations. When the more severe alterations are mentioned the descriptions are too brief for the understanding necessary for rational therapy.

Generally, the book is easy to read and it is well organized, with redundancy reduced to a minimum. Its greatest use should be as a handbook, for quick reference.

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